INDUSTRIAL MEDICINE *and* SURGERY

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feature issue....
LEAD CONFERENCE

MARCH 1959

Volume 28 Number 3

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1. Kuba, E. F.: First Stage Treatment of Burns and Prevention of Shock, Indust. Med. 12:369-371 (Aug.) 1958.

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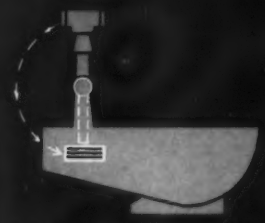

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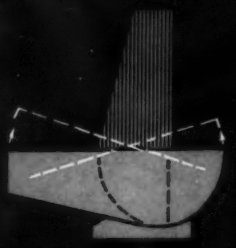

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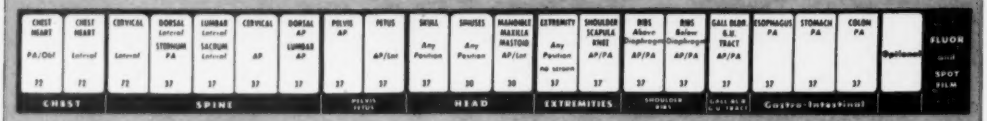

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INDUSTRIAL MEDICINE AND SURGERY

ESTABLISHED 1932

The International Journal of Medicine in Industry

MARCH, 1959
VOLUME XXVIII
NUMBER 3

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PERSONAL NEWS AND NOTES

WALTER J. GERSTLE, M.D. New Cumberland, Pennsylvania, a Public Health Physician, assumed duties as Director of Employee Health Service on November 20, 1958.

DR. GERSTLE came to this post in the Health Department's Industrial Hygiene Division from the Pennsylvania Railroad where, since 1943, he worked as a Medical Officer in various towns in Pennsylvania, Ohio and New York. A licensed practitioner in Pennsylvania, Massachusetts, Ohio and Wisconsin, he succeeds DR. ROBERT S. MUTCH who left the Health Service in September, 1958, to accept a position in West Virginia.

DR. GERSTLE earned his undergraduate degree at the University of Heidelberg, Germany, and received his professional degree from the University of Heidelberg's School of Medicine. He interned in Hamburg (Elbe) and took residencies in obstetrics and gynecology and in ear, nose and throat diseases in Berlin.

In the United States, he interned in hospitals in Altoona and Sewickley. Before accepting his Pennsylvania Railroad post, he studied for a year as a fellow in public health obstetrics in the Alabama State Health Department. He also has taken postgraduate work in the University of Pennsylvania Medical School's public health and preventive medicine department. He is a member of the Industrial Medical Association, American Association of Railway Surgeons, National Rehabilitation Association and American Medical Association.

Permanent Committee and International Association on Occupational Health, with the International Union of Pure and Applied Chemistry, will present the International Symposium on Maximum Allowable Concentrations of Toxic Substances in Industry, in Prague, Czechoslovakia, April 14-17, 1959.

The following Americans will address communications to the Symposium: ROBERT A. KEHOE, M.D., Cincinnati, Ohio; WILLIAM B. DEICHMANN, PH.D., F.R.S., Miami, Florida; WILLIAM P. YANT, SC.D., Pittsburgh and HARRY B. ELKINS, M.D., Boston.

INDUSTRIAL MEDICINE AND SURGERY

Instructions for Contributors

Manuscripts

Contributors should follow these simple instructions in the preparation of manuscripts.

All copy (including footnotes, references, quotations, etc.) should be typed *double-spaced* on one side only of 8½ by 11 inch good quality paper. Manuscripts and other materials for publication should be sent to John A. Lawrence, Managing Editor, *Industrial Medicine and Surgery*, P. O. Box 44-306, Miami 44, Florida.

Illustrations

Photographs should be unmounted, glossy prints about 8 by 10 inches and should be identified on the reverse side with the figure number and the author's name.

Drawings, charts, diagrams, graphs, etc. should be made with black India ink on good quality plain white paper.

References

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Proofs

Authors are sent galley proofs of their articles. These should be corrected and returned to the publication office as soon as possible. Reprints may be ordered when galley proof is returned.

Menninger Foundation holds its Fourth Annual Seminar for Occupational Physicians, March 2-6, 1959, in Topeka, Kansas. This seminar is for occupational physicians who are concerned with the health maintenance of a major segment of a company. It is designed to be helpful to those who recognize a need for orientation in the practical application of psychiatric knowledge and skills to their daily clinical activities.

Enrollment is held strictly to 20 physicians to assure the most effective learning experience possible.

The seminar objectives are to help the occupational physician further his understanding of psychological motivation, improve his skills in assessing the emotional aspects of medical problems, acquaint himself with techniques of brief psychotherapy, enlarge his knowledge of psychiatric treatment methods and criteria for referral, and develop a systematic point of view with respect to emotional influences on health.

The seminar will consist of three major units; Psychodynamics or Basic Theory of Psychological Motivation, Principles of Psychiatric Examination, and Psychiatric Treatment.

For additional information write: HARRY LEVINSON, PH.D., Director, Division of Industrial Mental Health, The Menninger Foundation, Topeka, Kansas.

Industrial Medicine and Surgery congratulates the following successful candidates for certification as Diplomates of the American Board of Preventive Medicine in the Occupational Medicine Division. The examination was held at the Industrial Health Conference, Atlantic City, April, 1958.

BERNARD BEHREND, M.D.; MERRILL P. BENOIT, M.D.; MERLE BUNDY, M.D.; J. GORDON BURDICK, M.D.; LAURENCE P. DEVLIN, M.D.; HILLIARD D. ESTES, M.D.; DENNIS J. FLYNN, M.D.; ROBERT JAMES HALEN, M.D.; HERMAN J. HALPERIN, M.D.; DAVID H. HERSH, M.D.; ERNEST Q. HULL, M.D.; HOWARD JOHN JOHNSON, JR., M.D.; BENJAMIN KAPLAN, M.D.; JOHN FRANK KILGUS, M.D.; CHARLES WILLIAM KRAUL, M.D.; PETER LEONE, M.D.; HALLETT A. LEWIS, M.D.; JOHN GABRIEL LIONE, M.D.; ERNEST MASTROMATTEO, M.D.; E. A. MCGOVERN, M.D.; JAMES J. O'HALLORAN, M.D.; GEORGE ALEX PODA, M.D.; JOHN A. PETERSON, M.D.; ROBERT JOSEPH POTTS, M.D.; JOHN H. STUNZ, JR., M.D.; R. B. SUTHERLAND, M.D.; JOSEPH B. TAUBER, M.D.; ERNEST ALDEN TERRY, JR., M.D.;* MATHILDA R. VASCHAK, M.D.; PETER VAUGHAN, M.D.; DOUGLAS J. WOOD, M.D.

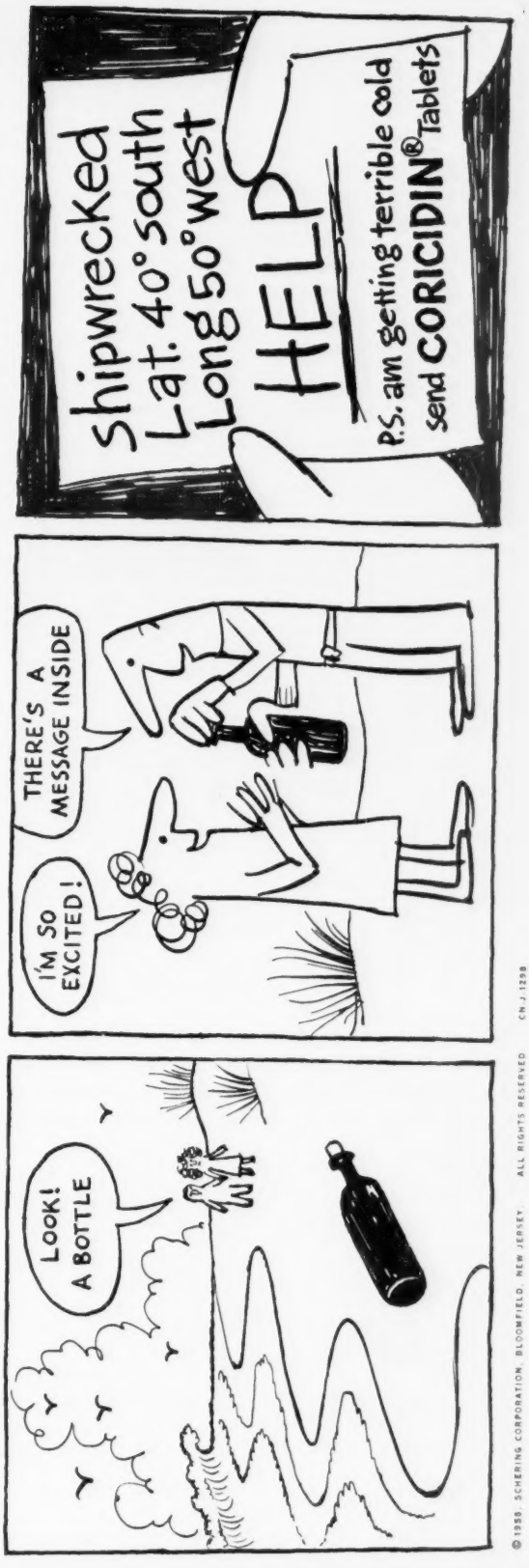
—*Deceased

WILLIAM A. FELLNER, M.D., was appointed Medical Director of General Motors Central Office, Detroit, Michigan.

DR. FELLNER will be in charge of the staff and facilities which furnish medical service to the employees of the Central Office and divisions located in the General Motors Building and Argonaut Building in Detroit.

He replaces WILLIAM J. FULTON, M.D., who retired February 1, 1959, under the provisions of the General Motors Retirement Program.

DR. FELLNER formerly was Medical Director of the Fisher Body Division plant in Pontiac, Michigan. He was graduated from the University of Michigan Medical School in 1953.



R. JAMES HERRON, M.D., has been named Medical Director of Pittsburgh Steel Co., Monessen, Pa.

He moves up from the position of Assistant Medical Director to succeed his late father, THOMAS B. HERRON, M.D., who died last December.

DR. HERRON will continue to make his headquarters at Monessen Works. He had been Assistant Medical Director since May, 1958.

He has been associated with Pittsburgh Steel since 1952. He also serves as a member of the surgical staff of Charleroi-Monessen Hospital. He is a member of the Westmoreland County and American Medical Societies, as well as the Industrial Medicine Society of Pittsburgh.

DR. HERRON completed undergraduate training at University of Pittsburgh and then graduated from Pitt's Medical School in 1943. He entered the U.S. Navy and served as a physician in the Pacific Theater before returning to civilian life in 1946. He also is a graduate of training in occupational and industrial medicine at New York University.

Third Annual Governor's Conference on Occupational Health was held at Memorial Hospital, University of North Carolina, Thursday February 5, 1959.

Appearing on the day-long program was FRED HENDERSON, Winston-Salem, chairman of the Governor's Council on Occupational Health; JOHN H. FOULGER, M.D., Wilmington, Del., Director of Medical Research, E. I. du Pont de Nemours & Co.; CHARLES WHITE, Upper Montclair, N. J., M & M Candies; GORDON HANES, Winston-Salem, Hanes Hosiery Mills Co.; STANLEY P. DELISSER, New York City, management consultant; ALAN MCLEAN, M.D., New York City, IBM Corp., and IRENE COURTENAY, Raleigh, N. C. State Board of Health.

HENDERSON presided at the meeting. DR. FOULGER spoke on "Occupational Health — An Economic Critique." "Does an Employee Health Program Pay Off in a Small Plant?" was WHITE'S subject. HANES used this same topic concerning large plants.

DELISSER spoke on "Controlling Costs of Absence." "Practical Application of Psychiatry in Industry" was DR. MCLEAN'S topic. MISS COURTENAY took part in an afternoon panel discussion with the speakers.

All of the details of the program were handled by the North Carolina Occupational Health Council, which was organized last year. After the council was created GOV. LUTHER HODGES requested it to assume the planning of these annual programs.

—From *Rocky Mount* (N.C.) *Telegram*, January 13, 1959.

Greater New York Association of Industrial Nurses, Inc., and Greater New York Safety Council will present "Minor Orthopedic Problems As Seen in the Industrial Medical Clinics," April 15, 1959, Hotel Statler, New York City. Moderator will be ANNA FERENCE, R.N., President, Greater New York Association of Industrial Nurses, Inc., and Assistant Executive Director, A.A.I.N. Program Chairman will be PAULINE WOHLRATH, R.N., Chief Nurse, The Port of New York Authority, New York City. Speaking on "Clinical Management" will be FREDERICK LEE LIEBOLT, M.D., Attending Surgeon in charge of Orthopedics, The New York Hospital, New York, N.Y. Speaking on "Preventive Measures" will be JAMES F. VAN NAMEE, Director Engineering & Research Division, Association of Casualty & Surety Company, New York, N.Y. and speaking on "The Why of How in Strain Prevention" (a demonstration) will be EUGENE SCHWARTZ, Senior Safety Representative, New York State Insurance Fund, New York, N.Y.

Second Asian Conference of Occupational Health was held in Calcutta, India, November 15-21, 1958, and in Jamshedpur, the steel town of India, November 22-23, 1958.

The following participated in the conference: delegates from Japan; delegates from China; delegates from Indonesia, delegates from the branches of the Society for the Study of Industrial Medicine, India, at Bangalore, Madras, Bombay, Ahmedabad, Delhi, Jamshedpur and Calcutta; The Ministry of Labour, Government of India; Ministry of Health, Government of India; Indian Army; Indian Air Force; delegate from Finland, Prof. Leo Noro; Representative from I.L.O., Dr. R. Murray; and representatives of employers. In all, 45 scientific papers were presented and discussed in detail.

At the business and organizational parts of the conference the basic constitution, as drawn up by Indian preparatory committee, was discussed. It was agreed that there was real need for a permanent organization that would bring together all workers in the field of occupational health in Asia. This will be discussed at the various national committees and final draft of the constitution of the proposed Association will be placed before the Third Asian Conference of Occupational Health.

World Health Organization-International Labor Organization combined conference was held at the All India Institute of Hygiene and Public Health at Calcutta, November 24-December 6, 1958.

The bulk of the work of the conference consisted of reading papers and group discussions on working papers submitted beforehand related to the three items of the agenda: 1. Occupational Health Services — definition, functions and organization. 2. Coordination in the field of occupational and industrial health, and 3. Teaching and training of occupational health.

The conference succeeded in drafting conclusions relating to many aspects of occupational health in the Southeast Asia.

Died

DONALD B. KNOWLES, M.D., 51, President of the Medical Staff of Roseland Community Hospital, was found dead Tuesday morning in his auto, apparently a victim of a heart attack.

DR. KNOWLES was head of the medical staff of the Acme Steel Co., Riverdale, and on the staff of Jackson Park Hospital.

He was President of the Chicago Society for Industrial Medicine in 1956.

A graduate of Northwestern University Medical School, he interned at St. Luke's Hospital.

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BOYD J. LARSEN, M.D., former works doctor for U.S. Steel's Geneva Works, has been named Medical Director for Utah Operations.

DR. LARSEN succeeds DR. MARTIN C. LINDEM of Salt Lake City, who will continue to serve Columbia-Geneva Steel in an advisory capacity. DR. SETH E. SMOOT, Utah county physician and specialist in industrial medicine, will replace DR. LARSEN as works doctor at Geneva. DR. LARSEN has studied at Brigham Young University, the University of Utah, and Washington School of Medicine at St. Louis.

—From *Salt Lake City* (Utah) *Deseret News*, January 8, 1959.

American Association of Railway Surgeons presents its 71st Annual Meeting, April 16-18, 1959, in the Drake Hotel, Chicago. The program is as follows: "Surgical Techniques in the Management of Pain" — OSCAR SUGAR, M.D., Chicago. "The Management of Melanomas" — EDWARD F. SCANLON, M.D., Evanston, Ill. "Indications and Limitations of Bronchoscopy in Lesions of the Lungs" — PAUL H. HOLINGER, M.D., Chicago. "A Statistical Study of Asymptomatic Pulmonary Infiltrations (Coin Lesions)" — JEROME R. HEAD, M.D., Chicago. Symposium on Peripheral Vascular Diseases — Moderator, DAVID I. ABRAMSON, M.D., Chicago; WILLIAM DYE, M.D., Chicago; PETER BEACONSFIELD, M.D., Chicago; JOHN H. OLWIN, M.D., Chicago. "Fractures of the Neck and Femur" — C. HOWARD HATCHER, M.D., Chicago. "Carotid Artery Disease" — PAUL ROSENBLUTH, M.D., Chicago. "Dissemination of Cancer Cells and Status of Radical Surgery in the Treatment of Cancer" — G. O. MCDONALD, M.D., Chicago. "The Hazards of Radiation" — ROBERT HASTERLIK, M.D., Chicago. "Recent Trends in the Development of Medical-Legal Claims" — ARTHUR H. CONLEY, M.D., Chicago. "Mental Depression — Diagnosis and Treatment" — BEN W. LICHTENSTEIN, M.D., Chicago. Symposium on Problems in the Management of Peptic Ulcer — Moderator, CLIFFORD J. BARBORKA, M.D., Chicago; G. GORDON MCHARDY, M.D., New Orleans; RICHARD D. MCKENNA, M.D., Montreal; EARL E. BARTH, M.D., Chicago; WALTER M. CARROLL, M.D., Chicago; J. M. DORSEY, M.D., Chicago. "Drug Hazards in Gastroenterology" — G. GORDON MCHARDY, New Orleans. "Management of Chronic Hepatitis and Hepatic Coma" — ROBERT J. BOLT, M.D., Ann Arbor, Mich. "Post-Traumatic Personality Disorders" — ALEX J. ARIEFF, M.D., Chicago; and NORMAN B. DOBIN, M.D., Chicago. "Contact Dermatitis" — JOHN B. HAEBERLIN, M.D., Chicago. "Recognition and Treatment of Pancreatitis" — LEO M. ZIMMERMAN, M.D., Chicago. "Present Day Evaluation of Antibiotics" — MARK H. LEPPER, M.D., Chicago.

Industrial Medical Association, American Industrial Hygiene Association, American Conference of Governmental Industrial Hygienists, American Association of Industrial Dentists, and American Association of Industrial Nurses, Inc. will participate in the 1959 **Industrial Health Conference,** April 25-May 1, 1959, Hotel Sherman, Chicago, Ill. This will be the 44th Annual Meeting of the Industrial Medical Association and their portion of the Conference will take place April 28-30. The program is as follows: "General Surgery Clinic" — B. C. KILBOURNE, M.D. "Fracture Clinic" — C. SCUDERI, M.D., or J. J. CALLAHAN, M.D. "Rehabilitation Clinic and Visit to Facility" — B. J. MICHELA, M.D. "Sappington Memorial Lecture" — CAREY P. MCCORD, M.D. "The Older Worker and Retirement" — NATHAN W. SHOCK, M.D. "Mental Health in Industry" — WILLIAM MENNINGER, M.D. and HARRY LEVINSON, PH.D. "The Interrelation of Medical Care Plans in Industry — The Windsor Plan" — R. B. ROBSON, M.D. "The Kaiser Medical Foundation" — H. A. LEWIS, M.D. "Hotel Trades Medical Center" — F. P. GUIDOTTI, M.D. "Coal Industry and the UMW Welfare and Retirement Fund" — J. D. WINEBRENNER, M.D. "Radioactive Sources, Discussion and Demonstration" — V. BEARD, PH.D. "Somatic Effects of Radiation" AUSTIN BRUES, M.D. "Periodic Chest X-Rays in Industry — Benefits Versus Radiation Hazards, Recommendations of the Radiation and Chest Committees of the IMA" — W. D. NORWOOD, M.D. "Radiation Protection Standards in Industrial Practice" — LAURISTON S. TAYLOR, PH.D. or WILLIAM MCADAMS, PH.D. "Arteriosclerosis, Hypertension, Coronary Disease — Current Concepts" — LOUIS N. KATZ, M.D. "Criteria of Aging — Clinical Aspects" — E. B. BAY, M.D.; "Psychological Testing" — W. C. HALSTEAD, PH.D. "Alcoholism in Industry — A Look at its Cause" — (two speakers). "Industrial Medicine — Some History and Background" — ALFRED H. WHITTAKER, M.D. "Medical Aspects of Motor Vehicle Accident Prevention" — H. BRANDELEONE, M.D. "Brachial Plexus Block for Hand Surgery — Experience at Henry Ford Hospital with 600 Cases" — J. W. DITZLER, M.D. "Reconstructive Treatment of the Crushed Hand" — M. L. MASON and J. L. BELL, M.D. "Operative Treatment of Juxta-Articular Fractures" — S. W. BANKS, M.D. "The Multiple Injury Problem" — C. SCUDERI, M.D. and J. J. CALLAHAN, M.D. "Industrial Medical Service In the Small Plant" — B. W. BROOKS, M.D. "Logic in Liability Settlements" CLEMENT MARTIN, M.D. "Drug Testing in Industrial Clinics" — H. E. TEBROCK, M.D. "The Impartial Medical Examiner in Workmen's Compensation" — SAM LEVINSON, M.D. and HARRISON MCLAUGHLIN, M.D. "The Rehabilitation Center's Function in a Community" — B. J. MICHELA, M.D. "Health Problems in Industrial Use of Plastics" — R. H. WILSON, M.D. "Beryllium Disease — Clinical Aspects" — HARRIET L. HARDY, M.D. and JOHN STOECKLE, M.D. "Experimental Studies" — A. J. VORWALD, M.D. "Toxicology of Agricultural Chemicals, Pesticides, Fertilizers, Etc." — MITCHELL R. ZAVON, M.D. "Cardiac Resuscitation in Industry" — R. M. HOSLER, M.D. "Follow-up of Inguinal Hernia Repair with Tantalum Mesh" — C. C. GUY, M.D. "Recurrent Thrombophlebitis" — D. I. ABRAMSON, M.D. "Occupational Skin Problems" — R. R. SUSKIND, M.D. "Gynecological Survey in Industry" — MAC ROY GASQUE, M.D. "Emotional Problems of Women in Industry" — S. G. ROGG, M.D.

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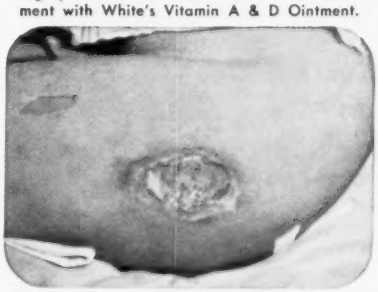

After daily treatment with White's Vitamin A & D Ointment—The sore is now filled with granulation tissue and shows signs of re-epithelization at margins.

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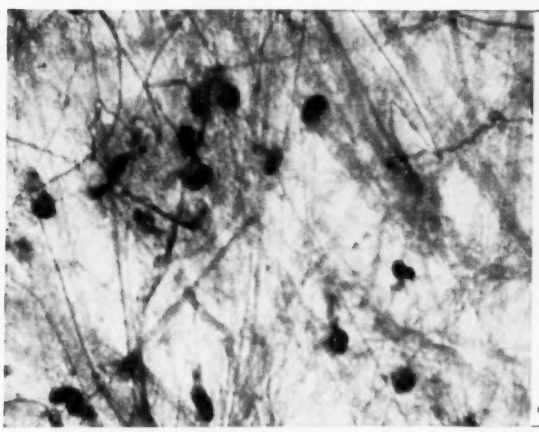
for relief of *chronic*—but *less severe* pain of rheumatic origin



Indications: Mild cases of rheumatoid arthritis, tenosynovitis, synovitis, bursitis, mild spondylitis, myositis, fibrositis, neuritis and certain muscular strains.

Dosage: Average initial dosage: 2 capsules 3 or 4 times daily. Maintenance dosage to be adjusted according to response.

Each Aristogesic Capsule contains:

ARISTOCORT® Triamcinolone	0.5 mg.
Salicylamide	325 mg.
Aluminum Hydroxide	75 mg.
Ascorbic Acid	20 mg.

Supply: Bottles of 100.

Collagen tissue (x250)

*TRADEMARK

Lederle

LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

In eczematous dermatitis with secondary infection CREME AND LOTION pH 5.0

COR-TAR-QUIN™

DOME

ACID MANTLE® • HYDROCORTISONE • STAINLESS TAR • DIIODOHYDROXYQUINOLINE

COR-TAR-QUIN is especially effective in those dermatoses where an inflammatory reaction is accompanied by increased scaling, lichenification, and secondary infection.

Combined hydrocortisone-coal tar therapy produces an enhanced antipruritic, anti-inflammatory response and diiodohydroxyquinoline is fungicidal as well as bactericidal. The Acid Mantle creme base of COR-TAR-QUIN helps restore and maintain normal pH of the skin. Relief is prompt and lasting.

Sig: Apply b.i.d. ½ oz., 2 oz., and 4 oz. tubes with either 0.5% or 1.0% hydrocortisone

INCORPORATED IN EXCLUSIVE ACID MANTLE® VEHICLE

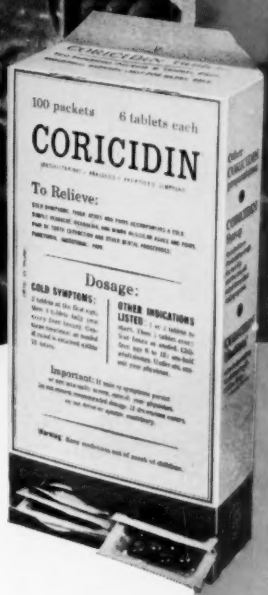
also available without the stainless tar, as CORT-QUIN™ CREME pH 4.5

A MOST TRUSTED NAME IN DERMATOLOGICALS

DOME CHEMICALS INC.

125 West End Avenue, New York 23, N. Y.
665 N. Robertson Blvd., Los Angeles 46, Cal.
2765 Bates Road, Montreal, Canada

to keep employees
on the job
put this to work



CORICIDIN
TABLETS

taken at work or at home
cuts down absenteeism due to

colds

dysmenorrhea

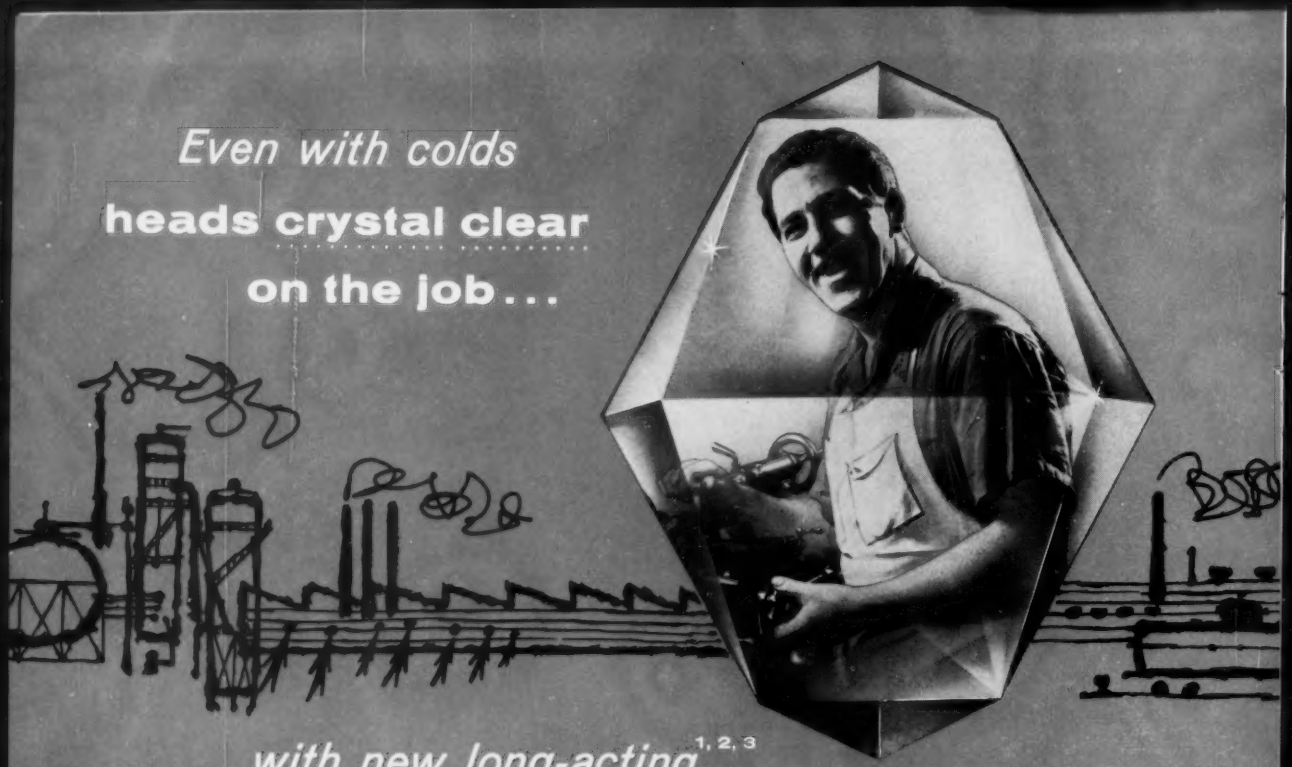
muscular aches and pains

Available in convenient industrial dispensing package containing 100 packets of 6 tablets each.

CORICIDIN,® brand of analgesic-antipyretic.

Schering

SCHERING CORPORATION · BLOOMFIELD, NEW JERSEY CN-J-619



Keeps heads clear 10-12 hours with a single oral dose with remarkable lack of side effects[1, 2]

DURABOND oral repository

DURABOND A new principle in medicine that controls absorption rather than dissolution or release, independently of gastrointestinal motility or specific pH. Maintains constant rather than sporadic blood levels, hence no over-release or under-release. This gives smooth therapeutic results, rare incidence of side effects.

RYNATAN TABULES for adults and older children

Rynatan contains:	Each tabule
Phenylephrine tannate	25.0 mg.
Prophenpyridamine tannate	37.5 mg.
Pyrilamine tannate	37.5 mg.

Dose: Tabules 1-2, every 12 hours . . . before work and at bedtime.

Neisler **IRWIN, NEISLER & CO.**
DECATUR, ILLINOIS

Available in Canada through
Lakeside Laboratories (Canada) Ltd., Toronto

Reduce absenteeism and inefficiency due to miseries of a cold, with Rynatan . . .

The first long-acting, oral, nasal and sinus decongestant—almost completely free from drowsiness and other side effects: ". . . of 311 patients, incidence of side effects was only 2.2 per cent. Evidence of sedation was (only) 1.2 per cent."[4]

Chemically and physically different. Employs no layers, enteric coatings, pellets, waxes or resins. Sustained action is built right into the molecule—with the Durabond principle.

1. Lawler, E.G. and Limperis, N. M.: Clin. Med. (Dec.) 1958. 2. Medical Science 3:376-377 (Mar. 25) 1958. 3. Cavallito, C.J. and Jewell, R.: J. Am. Pharm. A. (Scient. Ed.) 47:165-168, 1958. 4. Antibiotic Med. & Clin. Therapy 5:578-581 (Sept.) 1958.

FOR TRIAL IN YOUR OWN PLANT

Send for samples, clinical reprints and industrial prices.

IRWIN, NEISLER & CO.
INDUSTRIAL DIVISION—BOX 1110
DECATUR, ILLINOIS

Send information requested below:

_____ Samples and clinical reprints
_____ Industrial packaging and prices

Your Name_____ M.D.
Company_____
Plant Address_____
City_____ Zone____ State_____

no irritating steroid particles
The solubility of prednisolone acetate in water is 0.01 mg. cc. Suspended particles as shown are irritating to eye.
*The solubility of HYDELTRASOL—prednisolone 21-phosphate as the monosodium salt—is 675 mg./cc. or over 2000 times more soluble than prednisolone or hydrocortisone.

STERILE OPHTHALMIC SOLUTION

NEO-HYDELTRASOL®

(prednisolone 21-phosphate with neomycin sulfate)

2000 times more soluble than prednisolone or hydrocortisone*

- free of any particulate matter capable of injuring ocular tissues.
- uniformly higher effective levels of prednisolone.

SUPPLIED: Sterile Ophthalmic Solution NEO-HYDELTRASOL 0.5% (with neomycin sulfate) and Sterile Ophthalmic Solution HYDELTRASOL 0.5%. In 5 cc. and 2.5 cc. dropper vials. Also available as Ophthalmic Ointment NEO-HYDELTRASOL 0.25% (with neomycin sulfate) and Ophthalmic Ointment HYDELTRASOL 0.25%. In 3.5 Gm. tubes.
HYDELTRASOL and NEO-HYDELTRASOL are trade-marks of Merck & Co., Inc.

MSD

MERCK SHARP & DOHME
Division of MERCK & CO., INC., Philadelphia 1, Pa.

TWO NEW PARAFLEX* PRODUCTS

FOR RHEUMATISM AND TRAUMATIC DISORDERS

PARAFON*

THE SPECIFIC MUSCLE RELAXANT PLUS
THE PREFERRED ANALGESIC

FOR ARTHRITIS

PARAFON* with PREDNISOLONE

Effective and well tolerated on the practical dosage of only 6 tablets daily, PARAFON and PARAFON WITH PREDNISOLONE provide benefits that last for up to six hours.

PARAFON relieves pain, stiffness, and disability caused by rheumatism and traumatic disorders; PARAFON WITH PREDNISOLONE compounds this relief with anti-inflammatory action in treatment for arthritis.

supplied: PARAFON: Tablets, scored, pink, bottles of 50. Each tablet contains: PARAFLEX Chlorzoxazone† 125 mg.; and TYLENOL® Acetaminophen 300 mg.
PARAFON WITH PREDNISOLONE: Tablets, scored, buff colored, bottles of 36. Each tablet contains: PARAFLEX Chlorzoxazone 125 mg.; TYLENOL Acetaminophen 300 mg.; and prednisolone 1.0 mg.

precautions: The precautions and contraindications that apply to all steroids should be kept in mind when prescribing PARAFON WITH PREDNISOLONE.

*TRADE-MARK †U.S. PATENT PENDING

McNEIL

McNeil Laboratories, Inc • Philadelphia 32, Pa.

8R3A60

CYANAMID

SURGICAL PRODUCTS NEWS

NO. 1

INDIVIDUAL PLASTIC SUTURE PACKAGING HERALDS GREATER SAFETY FOR PATIENT AND PERSONNEL

Surgeon's Remarks Introduce New Film On Surgilope SP* Sterile Suture Strip Pack

The development of laminated plastic suture packaging has added another dimension to the security of patient care, according to Carl Walter, M.D., F.A.C.S. In an introduction to a new 20-minute film in sound and color which explains the Surgilope SP double-envelope sterile suture strip pack, the well-known Massachusetts surgeon points out many long-awaited benefits which the new package now makes possible.

New protection against cross-contamination

With the new Surgilope SP double-envelope strip pack, the sterile inner envelope containing the suture remains completely protected until delivered for use. There is no chance of contact with previously contaminated suture packages through storage in common jars and germicidal solutions. Since *no* known cold germicidal solution will kill the virus of hepatitis, the new double-envelope pack provides greater protection for the patient than was ever possible with ordinary packaging and storage methods.

Broken glass hazards eliminated

Additional benefits to both patient and O.R. personnel, through the elimination of glass suture tubes, are also cited by Dr. Walter. Since the suture nurse no longer fractures a glass tube to release the suture, the occupational risk of infection by homologous serum jaundice through cut gloves and fingers is done away with. The patient benefits because the suture cannot become contaminated with fragments of broken glass and its tensile strength is unimpaired by abrasion against the razor-sharp edge of the fractured tube.

Sutures reach surgeon in better condition

Because the plastic envelopes are quickly and easily opened at the last moment, deterioration due to exposure on the suture table does not occur and gut sutures do not stiffen and dry out. Further, the sutures are delivered in a loose coil rather than on the usual tightly-wound reel. As a result, the surgeon is more certain to receive a supple, kink-free, uniformly strong suture every time.

Complete line available

Both absorbable and non-absorbable sutures are available in the new Surgilope SP package. Materials include surgical gut, silk, nylon, polyethylene, cotton, and stainless steel. Sutures are packaged either ready-armed with Atraumatic® needles or as standard and pre-cut lengths. Hospitals can now standardize on Surgilope SP sutures and completely eliminate jars, storage solutions and the nuisance of different preparation technics.

O. R. Nurses find change-over easy

Because of the simple preparation technic, the change to the new suture package presents no problems to the hospital. In a matter of minutes nurses can learn to strip open the outer envelope and serve the sutures quickly and correctly. Three safe and efficient methods of dispensing Surgilope SP sutures are available: circulating nurse technic, drop technic and circulating to suture nurse technic. This choice of practical technics assures a variation suitable to every operating room situation and maximum efficiency under all circumstances.

Film available for hospital showings

The new sound and color film describing the use and advantages of the Surgilope SP plastic double-envelope suture package—with comment by Dr. Carl Walter—is now available for showings to hospital audiences, medical societies and other interested groups. Arrangements may be made through local Surgical Products Division representatives, or by writing to American Cyanamid Company, Surgical Products Division Sales Office, Danbury, Connecticut.

*Trademark

New CURON† Elastic Foam Bandage Has Unique Advantages

"One of the most important recent developments in the elastic bandage field!" That's been the reaction of one physician after another on trying the new Curon elastic foam pressure bandage.

Since its introduction at the Chicago meeting of the American College of Surgeons late last year, Curon's unique properties have brought it rapid acceptance throughout the medical profession.

A totally different type of pressure bandage, Curon is composed entirely of a newly developed, highly porous plastic. It contains no fabric, no rubber ... may be washed and autoclaved without deterioration, and is physiologically inert. Because it clings to itself, Curon is exceptionally easy to apply, even in hard-to-bandage areas. This same property helps it to stay neatly in place where other elastic bandages tend to slip or creep.

Extremely elastic, Curon permits precise regulation of tension to meet individual requirements. Its surprising lightness and unique porosity help speed healing and greatly enhance patient comfort.

The new Curon bandage is available in 2″, 3″, 4″ and 6″ widths, individually boxed in 3 yard rolls. Readers wishing to place an initial order may do so through their Surgical Products Division Representative, surgical supply dealer, or by writing direct.

†*Curtiss-Wright Corporation's registered trademark for their plastic foam used in this bandage*

ANNOUNCE VIM® DISPOSABLE SYRINGE AND NEEDLE LINE

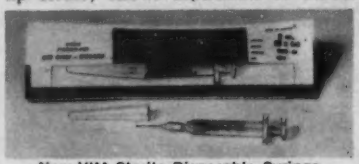
Meets Demand For Better Performance At No Increase In Cost

The introduction this year of a complete line of sterile-packed Vim disposable syringes and needles, as well as a sterile Economy Needle line, climaxes a unique development program. Physicians and hospitals surveyed on the cross-infection problem showed a continuing desire for better-functioning, more economical disposable hypodermic equipment. Hundreds of comments and criticisms on existing "disposables" were catalogued and the new Vim line was literally "designed to order" to meet ideal specifications.

Vim disposables offer precision performance

The new Vim disposable syringes and needles incorporate many improved construction and performance features. For example, the point of the Vim disposable needle has new side bevels and is so sharp that it actually penetrates tissues more easily than many standard needles. The cannula is heavy-gauge stainless steel, rugged enough to safely resist bending or breaking and certain not to rust before use. The cannula is *fused*—not simply glued—to the plastic hub to provide new protection against breaking or leakage at this vulnerable spot. The hub is square, like standard needles, for easier handling. It is precision molded to guarantee a leak-free fit on any standard or disposable syringe and is easily removed from the syringe after use. Vim disposable needles are packaged in a new, individual snap-open pack of clear, durable wet-proof plastic.

The new Vim disposable syringe closely matches the heft, feel and satin-smooth action of the finest Vim standard syringes. Made of heavy-duty, chemical-resistant Cymac® plastic—a new development of American Cyanamid research—the syringe has the weight, balance and length ideal for convenient use. Because barrel and plunger are molded of the same material a perfect fit without "wobble" or "backfire" is assured. Accurate, easy-to-read calibrations and flat plunger end assure precise dosage. Transparent Luer tip clearly shows aspiration of blood.



New VIM Sterile Disposable Syringe is a precision instrument

The new Vim disposable syringes and needles—sterile-packed in strong, fast-opening polyethylene envelopes—are available separately or as complete syringe-and-needle units.

Economy needle line offered

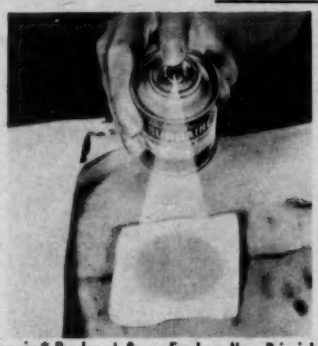
To fill the gap between the standard and fully disposable Vim lines, Surgical Products Division has also announced a special Economy Needle. Packaged sterile in the new snap-open plastic pack, it is suitable for one-time use, but because of its metal hub and rugged, stainless cannula it may be re-sterilized and used again. The Economy Needle provides the benefits of new-needle sharpness for limited use and is inexpensive enough to be discarded before time-consuming resharpening is required.

VIM Sterile Disposable Needle comes in all-plastic, snap-open pack

Lower costs achieved

In developing the Vim disposable lines, much attention was given to perfecting more efficient manufacturing technics. As a result, production costs have been controlled despite the many higher quality features which the new products incorporate. The new Vim disposables actually sell at prices comparable to, or even lower, than those of present disposable brands. And for hospitals that take advantage of the extra discounts possible with the Surgical Products Division Direct-Purchase Plan even greater savings are possible.

CHECKS WOUND ODOR AT SOURCE!



Surgaire® Deodorant Spray Employs New Principle

Positive control of the most offensive wound odor for more than 12 hours per application is now possible with Surgaire, a new sterile aerosol deodorant introduced by Surgical Products Division.

Unlike spray or wick-type deodorants which merely mask airborne odors with their own strong scent, Surgaire is designed to be sprayed directly on the dressing covering the wound. Acting at the source, it checks odor by chemical action *before* it can permeate the air of the sick room. Employed routinely wherever wound odor is a problem, this effective, easily applied deodorant can do much to improve morale of patient and attending personnel in hospitals, nursing homes, cancer clinics, as well as in the home.

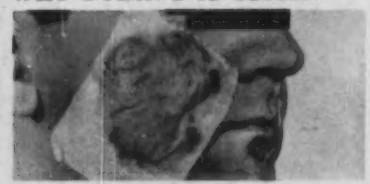
CYANAMID

AMERICAN CYANAMID COMPANY
SURGICAL PRODUCTS DIVISION
NEW YORK, N. Y.

SALES OFFICE: DANBURY, CONNECTICUT

®Trademark

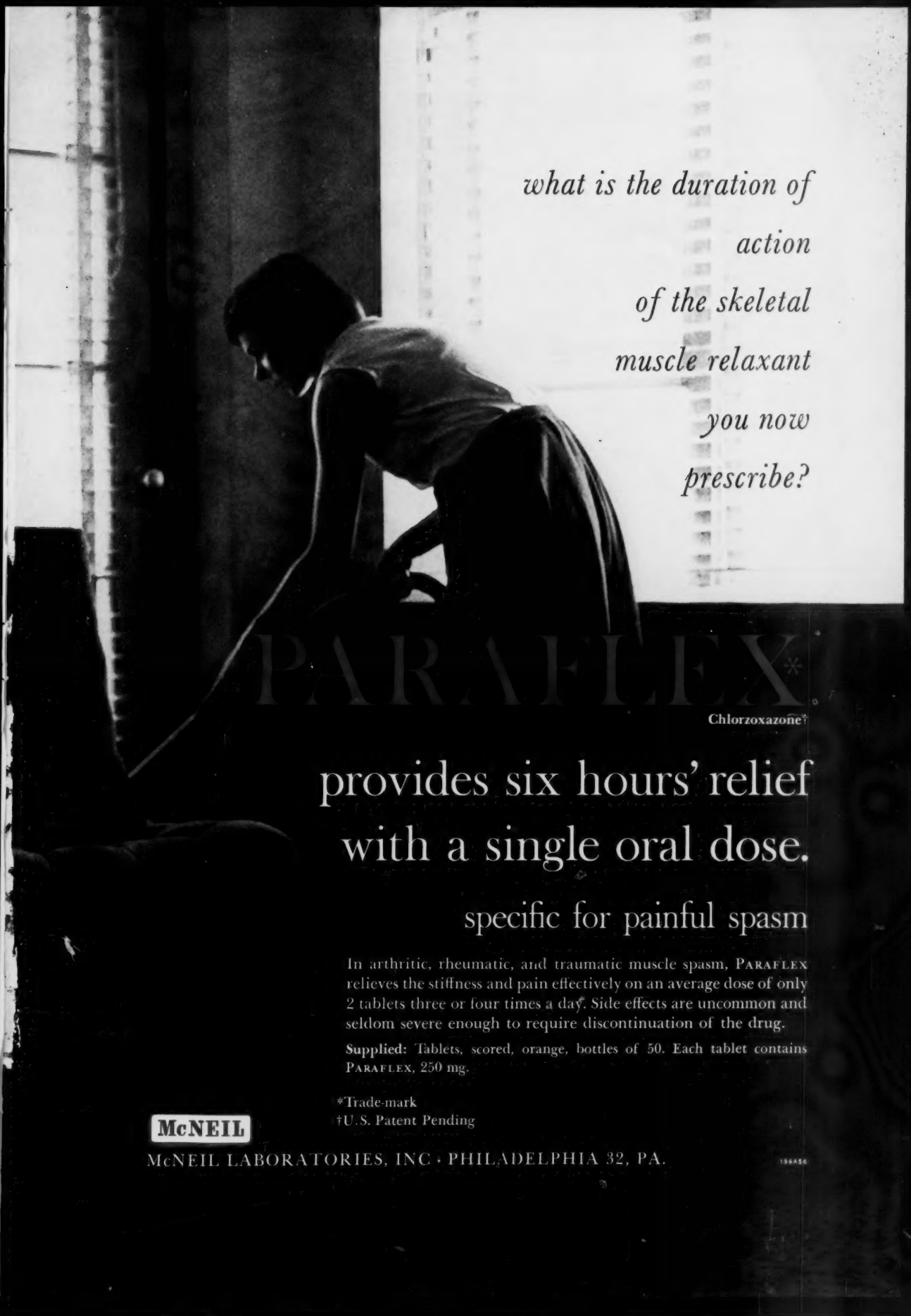
WHY DOESN'T IT STICK?



"MICROGAUGE" MESH IS KEY TO SUCCESS OF NEW OWENS® STERILE NON-ADHERENT DRESSING

Hailed as an important advance in wound dressing technic, Owens contact dressing prevents wound adherence *without* occlusive ointments or other impermeable wound coverings! The dressing's unique "microgauge" mesh effectively bars capillary penetration, yet allows liquid exudates to pass freely.

Owens Non-Adherent Dressing has been used for 4 years in leading hospitals to hasten healing and improve cosmetic result on burns, granulating areas, skin graft donor sites, and surface wounds. Now available sterile, in individual envelopes, Owens Dressings are ideal for routine hospital, office and emergency use to improve healing and minimize painful tearing of wound surfaces. Dressings are supplied Plain, or Neomycin-Treated for infected or potentially infected surfaces. Both types come in 3" x 8" and 8" x 12" sizes.


what is the duration of
action
of the skeletal
muscle relaxant
you now
prescribe?
PARAFLEX*
Chlorzoxazone†
provides six hours' relief
with a single oral dose.
specific for painful spasm
In arthritic, rheumatic, and traumatic muscle spasm, PARAFLEX relieves the stiffness and pain effectively on an average dose of only 2 tablets three or four times a day. Side effects are uncommon and seldom severe enough to require discontinuation of the drug.
Supplied: Tablets, scored, orange, bottles of 50. Each tablet contains PARAFLEX, 250 mg.
*Trade-mark
†U.S. Patent Pending
McNEIL
McNEIL LABORATORIES, INC. • PHILADELPHIA 32, PA.
196A56

with **BUFFERIN® IN ARTHRITIS**

salicylate benefits with minimal salicylate drawbacks

Rapid and prolonged relief—with less intolerance.

The analgesic and specific anti-inflammatory action of BUFFERIN helps reduce pain and joint edema—comfortably. BUFFERIN caused no gastric distress in 70 per cent of hospitalized arthritics with proved intolerance to aspirin. (Arthritics are at least 3 to 10 times as intolerant to straight aspirin as the general population.[1])

No sodium accumulation. Because BUFFERIN is sodium free, massive dosage for prolonged periods will not cause sodium accumulation or edema, even in cardiovascular cases.

Each *sodium-free* BUFFERIN tablet contains acetylsalicylic acid, 5 grains, and the antacids magnesium carbonate and aluminum glycinate.

Reference: 1. J.A.M.A. 158:386 (June 4) 1955.

ANOTHER FINE PRODUCT OF BRISTOL-MYERS

Bristol-Myers Company, 19 West 50 Street, New York 20, N. Y.

***The most comfortable patients with hemorrhoids are those who use* Nupercainal®** *Ointment or Suppositories*

NUPERCAINAL relieves intense itching, burning and pain during non-surgical treatment of hemorrhoids. Used postoperatively, it promotes lasting comfort. Also useful for routine office instrumentation, cuts, minor bruises, sunburn and whenever a topical anesthetic is indicated. Does not contain narcotics to mask serious rectal disease.

NUPERCAINAL *Ointment*, 1% (petrolatum base); 1-ounce tubes with rectal applicator, and 1-pound jars for office use.

For convenience and accurate control of dosage: NUPERCAINAL® *Suppositories*, 2 Gm., each containing 2.5 mg. Nupercaine® (dibucaine CIBA) base; boxes of 12.

NUPERCAINAL® (dibucaine CIBA)

CIBA
SUMMIT, N. J.

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NOW many more hypertensive patients may have THE FULL BENEFITS OF CORTICOSTEROID THERAPY

Except for one case of mild blood-pressure elevation (150/90) **no hypertension was seen in any of 1500 patients†** as a result of treatment with DECADRON—the new and, on a milligram basis, most potent of all corticosteroids. **Hypertension induced by other steroids diminished or disappeared.**

Thus with DECADRON, hypertension no longer appears to be a contraindication to successful corticosteroid therapy. And the dramatic therapeutic impact of DECADRON was virtually unmarred by diabetogenic or psychic reactions . . . Cushingoid effects were fewer and milder . . . and there were no new or "peculiar" side effects. Moreover, DECADRON helped restore a "natural" sense of well-being.

†Analysis of clinical reports.

Decadron* DEXAMETHASONE

treats more patients more effectively

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MERCK SHARP & DOHME
DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.

VERSATILE FURACIN

effective by intrapleural instillation[1]

the situation: Four-month-old infant with staphylococcal pneumonia and empyema resistant to most antibiotics was allergic to antibiotic chosen after sensitivity tests. Thoracentesis produced 30-40 cc. of creamy, purulent fluid. Organism was Staphylococcus aureus, coagulase positive.

then Furacin was instilled: 0.2% Solution was diluted equally with physiologic saline and 10 cc. of mixture instilled twice daily into pleural space, with suction catheter clamped off for 1 hour. Fluid almost immediately became thinner and less viscous. Twenty-four hours later infant was less irritable, voluntarily started taking food. Instillations stopped. FURADANTIN® Oral Suspension prescribed. Recovery uneventful.

1. Perkins, J. L.: Kansas State M. J. (to be published).

FURACIN®

brand of nitrofurazone

FURACIN has been in clinical use for more than 13 years. Today it is the most widely prescribed single topical antibacterial agent. Like other nitrofurans, FURACIN remains effective, even in pus, sera or exudates, against pathogens which have developed—or are prone to develop—resistance to antibiotics.

FURACIN, in a water-miscible base of polyethylene glycols, is available in a number of dosage forms. Included are Soluble Dressing, Soluble Powder, Solution and Cream. Also in Vaginal Suppositories, Inserts, and in special formulations for eye, ear and nose.

NITROFURANS—a unique class of antimicrobials—neither antibiotics nor sulfonamides

EATON LABORATORIES, NORWICH, NEW YORK

found effective in relieving

ITCHING OF ALLERGIC REACTIONS

...in 77% of all cases

Temaril* *Tablets Syrup*

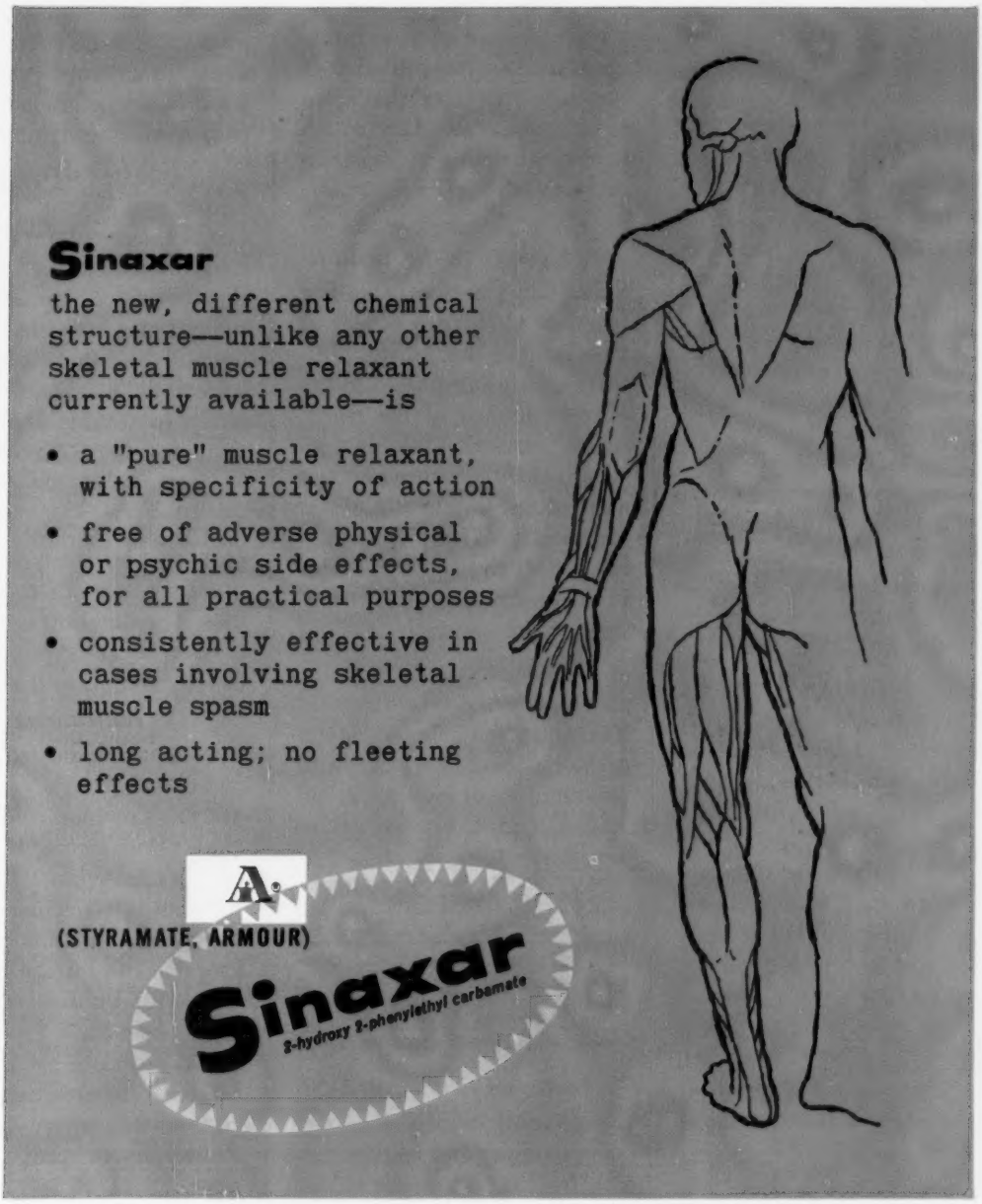
relieves itching... regardless of cause

Tablets, 2.5 mg., in bottles of 50.
Syrup, 2.5 mg./5 cc. tsp., in 4 fl. oz. bottles.

Smith Kline & French Laboratories

*T.M. Reg. U.S. Pat. Off. for trimeprazine, S.K.F. [*dl*-10-(3-dimethylamino-2-methylpropyl)-phenothiazine]

DISAPPOINTED with skeletal muscle relaxants that cause GI distress, drowsiness, and dizziness.....


Sinaxar
the new, different chemical structure—unlike any other skeletal muscle relaxant currently available—is
• a "pure" muscle relaxant, with specificity of action
• free of adverse physical or psychic side effects, for all practical purposes
• consistently effective in cases involving skeletal muscle spasm
• long acting; no fleeting effects
A
(STYRAMATE, ARMOUR)
Sinaxar
2-hydroxy 2-phenylethyl carbamate

ARMOUR PHARMACEUTICAL COMPANY • KANKAKEE, ILLINOIS / *a leader in biochemical research*

Physicians turn to Tessalon® to control cough

Single agent with multiple actions broadens cough therapy

A single therapeutic agent developed by CIBA research now does all that has been attempted with combination cough remedies. Extensive clinical trials, in this country and abroad, involving more than 3,000 patients with acute or chronic cough, show that TESSALON *has at least six advantages* that result in the better total management of the patient with cough:

1. TESSALON acts peripherally, to control cough where cough begins—in the chest.
2. TESSALON acts centrally, to control cough at the level of the "cough center" in vagal nuclei in the medulla.
3. TESSALON thins sputum.[1]
4. TESSALON increases vital capacity and ventilation.
5. TESSALON improves exercise tolerance.
6. TESSALON relieves dyspnea, wheezing, "blackouts."

Fewer coughs per minute

Shane and co-workers,[2] using the method of Bickerman and Barach,[3] induced measurable cough in 20 volunteers; a 15 per cent citric acid aerosol was used as the cough-producing agent and each volunteer was tested on three different occasions. The antitussive efficacy of TESSALON (100 mg.) was estimated to be 2½ times that of codeine (½ grain) in this test.

Cough suppressing activity of TESSALON[2]

	Average number of coughs*
No therapy	8.3
Codeine	4.4
TESSALON	1.7

*Based on 5-minute interval immediately following inhalation of citric acid to induce cough. Each patient underwent this test on three separate occasions.

Controls cough in the chest

It has been shown that the increased sensitivity of the sensory receptors in the lung during inspiration is an important part of the cough mechanism. TESSALON has a selective inhibiting effect on these dilation or "stretch" receptors[4] that helps to control cough where cough begins—at points of irritation in the chest.

Controls cough at the cough center in the medulla

Spinal reflex arcs were studied for the inhibitory effect of TESSALON on the transfer of afferent cough impulses to the efferent branch of the cough reflex.[5] TESSALON inhibited reflex transmission, when the afferent nerve was stimulated electrically. With this "damping" effect on the cough center in the medulla, TESSALON controls cough centrally, as well as peripherally.

Thins sputum

TESSALON controls cough frequency without interfering with productivity or expectoration. In fact, sputum is usually thinner, easier to raise.[1]

Effect of TESSALON on sputum[1]

Amount		Consistency	
Less	32 patients	Heavier	3 patients
More	2* patients	Lighter	27 patients
Same	16 patients	Same	20 patients

*These patients noted more but lighter sputum.

Increases vital capacity

Respiration usually increases both in depth and volume during TESSALON treatment.[6] In one study,[7] patients with chronic respiratory disease, with and without bronchospasm, showed a mean increase of 19.7 per cent in vital capacity after a 2-week course of TESSALON.

Improves exercise tolerance

By inhibiting stretch receptor activity, and by increasing air intake, TESSALON enables patients to tolerate exercise or work better, eliminates many paroxysms of coughing.

Relieves dyspnea

Farber and Wilson[8] note that one of the important contributions of TESSALON to cough therapy is "... its action as a reliever of dyspnea in some patients." Shortness of breath, wheezing, "blackouts" are not likely to trouble the patient treated with TESSALON.

Fast, prolonged action

The cough suppressant effect of TESSALON starts rapidly — usually within 15 to 20 minutes. The duration of the antitussive effect is prolonged — usually from 3 to 8 hours.

Indications

TESSALON is indicated in acute and chronic cough.

ACUTE: Common cold • Bronchitis • Pneumonia • Upper respiratory infection • Pleurisy • Spontaneous pneumothorax • Bronchial irritation provoked by gases and foreign bodies

CHRONIC: Pulmonary emphysema • Bronchitis (emphysematous, asthmatic) • Bronchial asthma • Tuberculosis • Other chronic pulmonary diseases • Pulmonary or mediastinal tumors

PROCEDURES: Bronchoscopy and bronchography • Thoracentesis • Thoracic surgery

Dosage

ADULTS: Average dosage is one Perle (100 mg.) t.i.d. If necessary, or where cough is refractory, up to 6 Perles (600 mg.) daily may be given.

CHILDREN UNDER 10: One Pediatric Perle (50 mg.) t.i.d. is the usual dosage.

The Perles should be swallowed without chewing, and, if necessary, with a liquid. Release of TESSALON from the Perle in the mouth produces a temporary local anesthesia of the oral mucosa.

Side Effects

TESSALON is well tolerated. Only occasionally have side effects been reported. Skin rash, nasal congestion and a vague "chilly" sensation have been mentioned. In rare instances, gastrointestinal upset, constipation or sedation have been observed. No adverse effects on respiration, kidney or liver function tests, blood count or urinalysis were reported.

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Samples available on request.

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1. Simon, S. W.: Ann. Allergy 15:521 (Sept.-Oct.) 1957. 2. Shane, S. J., Krzyski, T. K., and Copp, S. E.: Canad. M.A.J. 77:660 (Sept. 15) 1957. 3. Bickerman, H. A., and Barach, A. L.: Am. J. M. Sc. 228:156 (Aug.) 1954. 4. Bein, H. J., and Bucher, K.: Helvet physiol. et pharmacol. acta 15:55 (March) 1957. 5. Meier, R., and Bein, H. J.: Personal communication. 6. Michelson, A. L., and Schiller, I. W.: J. Allergy 28:514 (Nov.) 1957. 7. Bickerman, H. A.: To be published. 8. Farber, S. M., and Wilson, R. H. L.: To be published.

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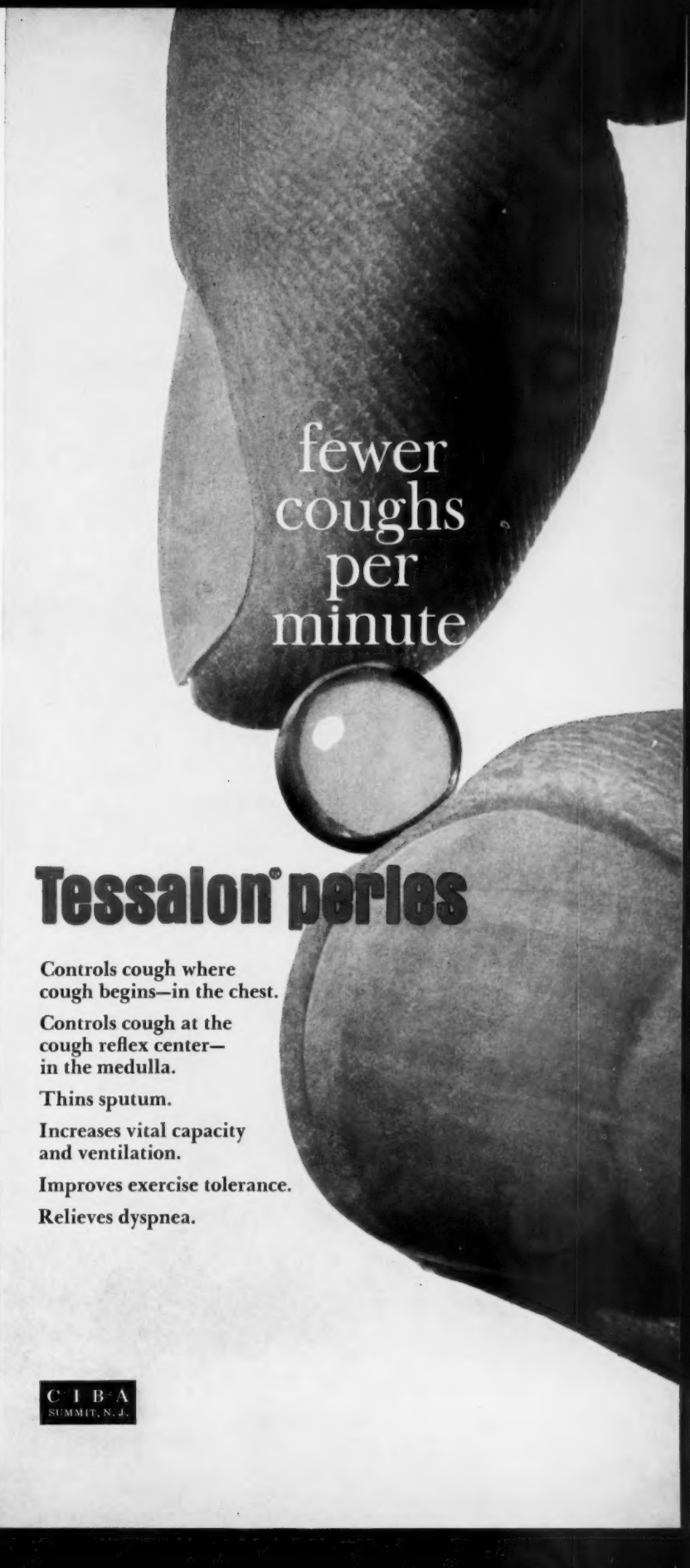

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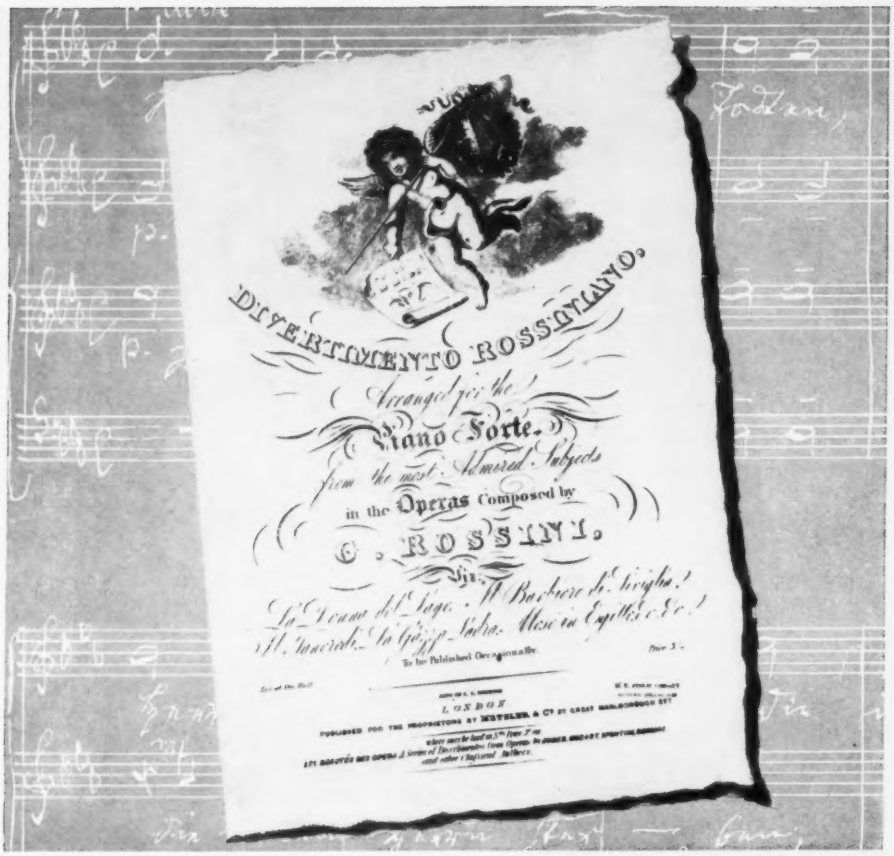
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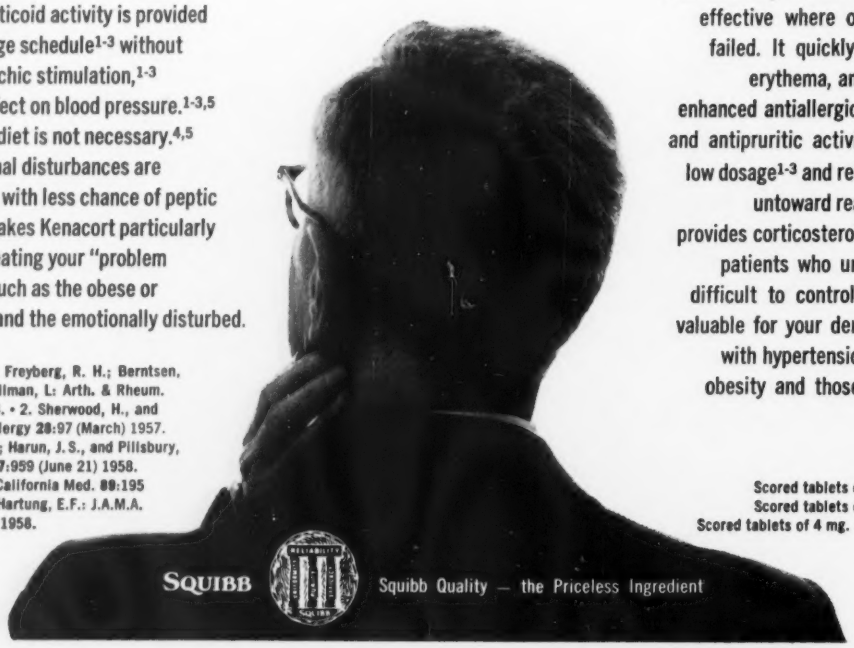

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References: Annals of Allergy, Vol. 6. July-August 1948. Study of a New Histamine Antagonist, The Pennsylvania Med. J., Vol. 51. Clinical Study of a New Antihistaminic Drug—Phenindamine. Dristan Clinical Study.

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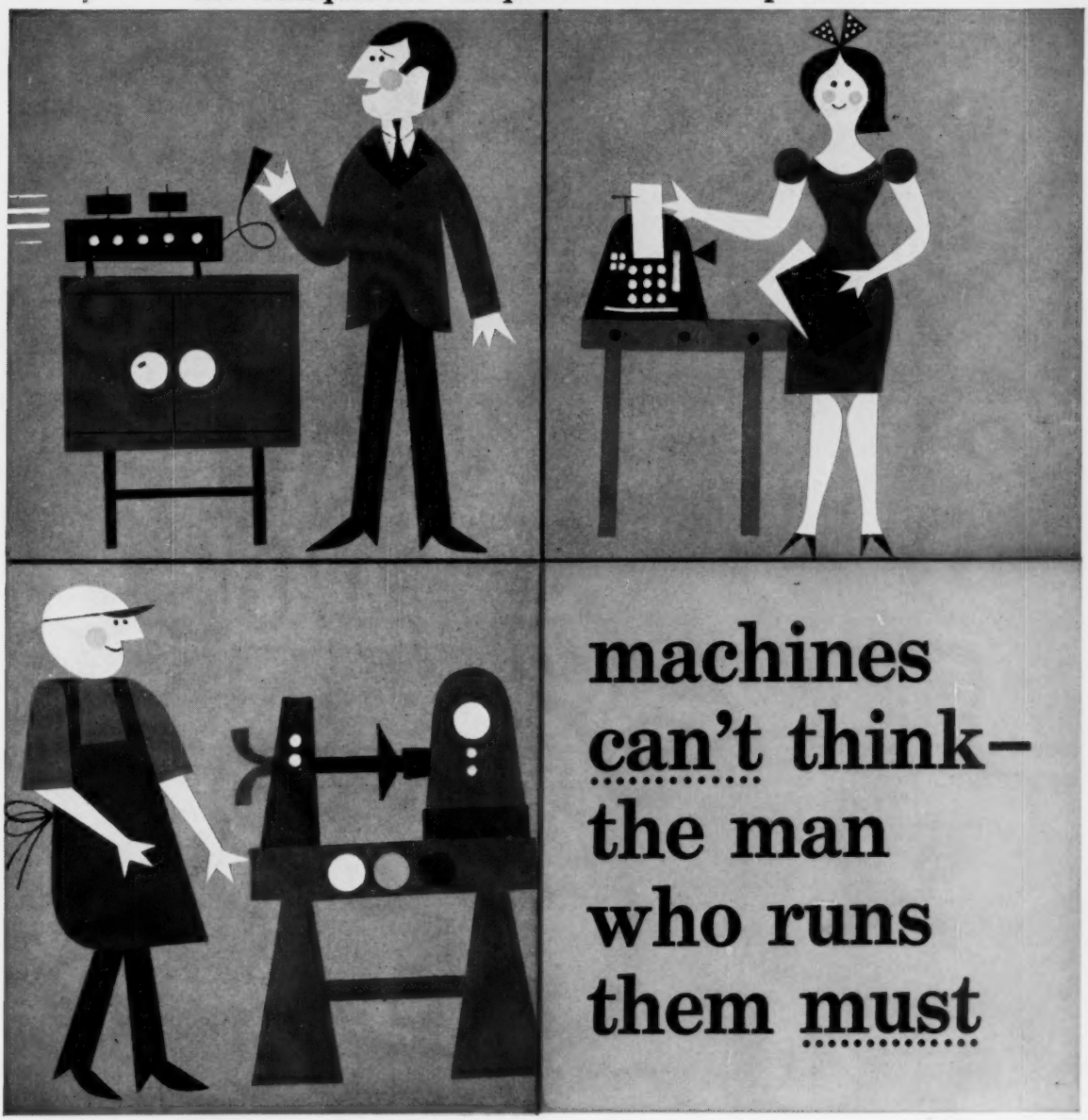

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References: 1. Ayd, F. J., Jr.: New York J. Med. *57*:1742 (May 15) 1957. 2. Bayart, J.: Presented at the International Congress of Pediatrics, Copenhagen, Denmark, July 22-27, 1956. 3. Cohen, S.: Am. Pract. & Digest Treat. *8*:946 (June) 1957.

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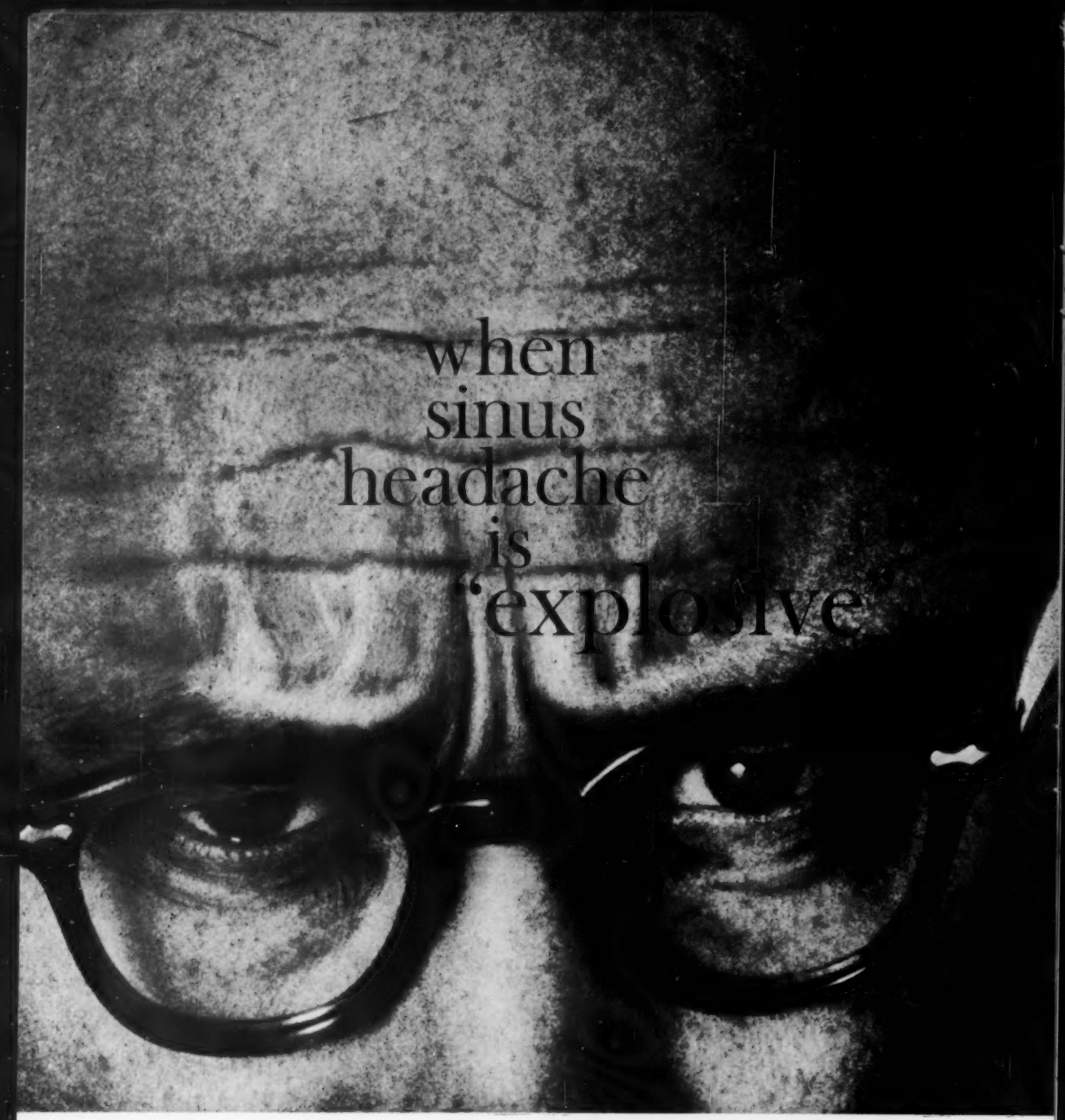

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REFERENCES

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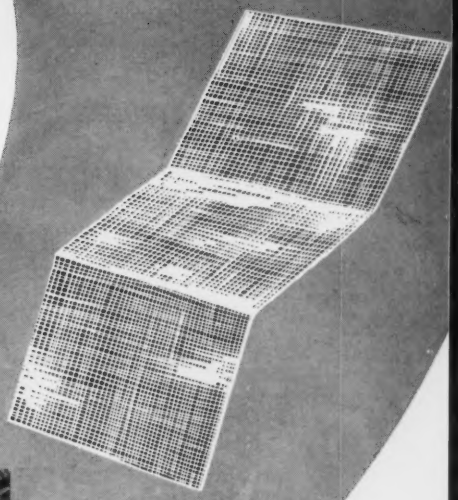

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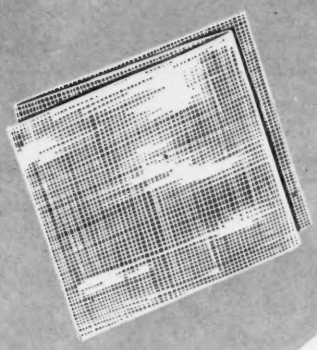

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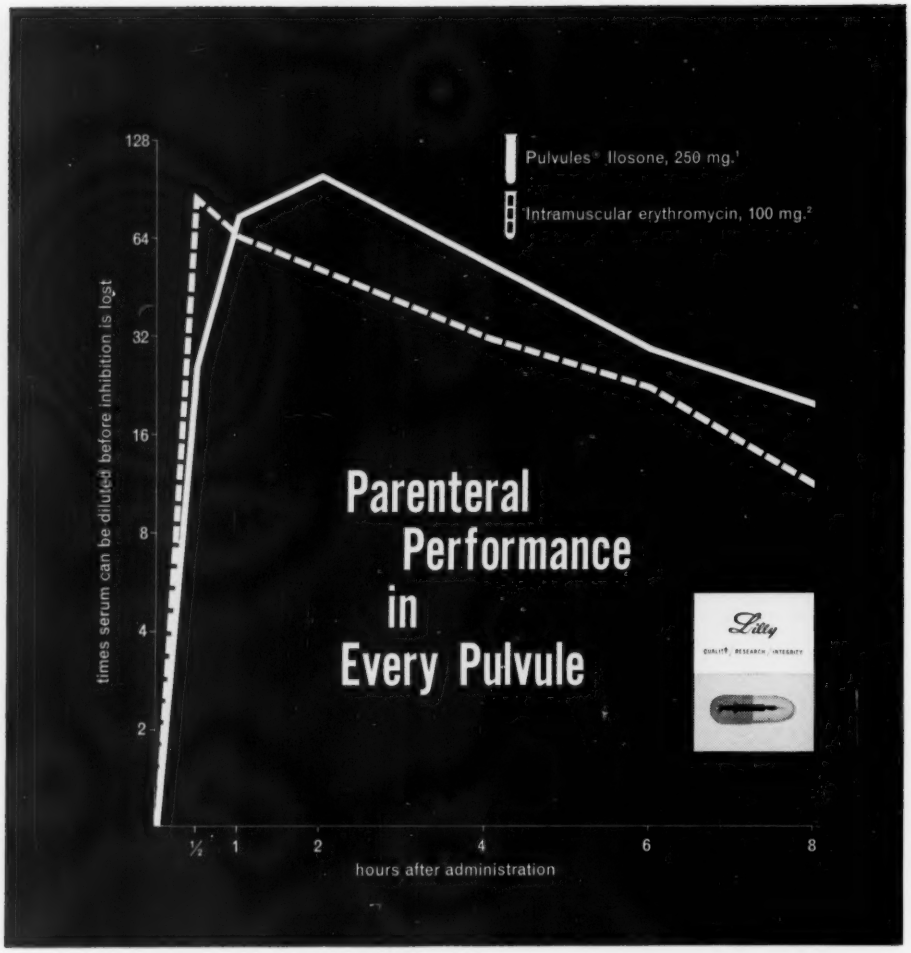

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1. Antibiotic Med. & Clin. Therapy, 5:609, 1958.

2. Data from Antibiotics Annual, p. 269. 1954-1955.

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IMS

The Lead Hygiene Conference

Lead Industries Association
November 6-7, 1958
Chicago, Illinois

The same genius that provided greatness for the lead industries of the land has been applied in the protection of lead handling workers. The Lead Industries Association, never blind nor even myopic, long has accepted the potential perils in lead and its compounds and has accepted leadership in keeping these perils potential and not actual. To this end was created the Association's Division of Health and Safety. Wherever and however lead is utilized, the workers involved become the concern of that protective division.

The highwater mark of the Health and Safety Division's activities is to be found in the highly occasional "Lead Hygiene Conferences." These conferences bring together the qualified minds of the country most likely to reach a consensus as to optimal measures in the prevention, the detection and the therapy of lead poisoning.

This featured issue of this Journal constitutes the proceedings of the latest conference. The list of topics indicates full freedom of the numerous speakers as to their presentations. By all it was agreed that lead can cause catastrophe, but lead's threat is subject to ready control. Clinical lead poisoning on a comparative basis, now has become a rarity, but the ominousness of lead poisoning is a reality. The target of this conference, of which this is the record, was the threat — the "what might happen."

These same proceedings, under the Association's imprint, in due course will become available. Copies of these records will be obtainable from Lead Industries Association, 60 East 42nd Street, New York 17, New York.

The first session of the Lead Hygiene Conference of the Lead Industries Association convened at 10 o'clock in the Grand Ballroom of the Drake Hotel, Chicago, Illinois, with Mr. Manfred Bowditch, Director of Health and Safety, Lead Industries Association, presiding.

—The Editors

CLINICAL CONTROL of HEALTH

in the Storage Battery Industry

• ELSTON L. BELKNAP, M.D., and
• ELSTON L. BELKNAP, JR., M.D.
Milwaukee, Wisconsin

When the senior author was first engaged as a consultant medical director of a large battery company in 1930, the general manager asked that management be advised once a month regarding the level of lead absorption in the workers. He also said, "Make your recommendations ideal — aim at the stars for what you think should be done to prevent lead absorption but don't be surprised if we don't put into effect all the recommendations at once. However, keep after us and gradually we will put them into effect as soon as we can work them into our production schedules." Over the years, the company and their insurance carrier have been slowly but faithfully improving protective engineering ventilation designed to collect lead dust at its source. The company is Globe Union, Inc., and the insurance carrier, Employer's Mutual of Wausau.

Both by frequent plant tours and their correlation with physical and laboratory examinations of the men, the Medical Department has been able to point out definite points at work places where production equipment was defective or inadequate regarding dust collection, thus causing increased lead absorption. However, with the increasing speed of modern machines, the potential lead hazard has been multiplied rapidly. In most instances we have all felt that we were working as a team — foreman, superintendent, engineers, general manager and the lead-exposed workmen themselves — as well as the Medical Department, in a determined effort to reduce human lead absorption as rapidly as practical.

The result of this teamwork is demonstrated by the reduction of the rate of disabling lead intoxication from 20% in 1929 to 2% or 3% within the first six years, and by the fact that thereafter disabling lead intoxication or true lead poisoning has averaged only one every other year, and none at all the last two years. All of these cases were of the simple lead colic type and were never complicated with lead palsy or encephalopathy. (Figure 1)

The year 1929 was known to some of you as the great financial crash. That was the year just before I came to the company when there was the greatest incidence of disabling lead intoxication. Then it tapered off fairly rapidly when we sorted out our most heavily exposed workers and had a very cooperative engineering group working to reduce the lead exposure. There was a long period, from 1935 to 1950, when we had only one case of lead intoxication.

Again in 1955, there was a peak of five cases. This was the time when automobile production the country over was at its peak, and we were working in many instances 10 hours a day, six days a week, all contributing to increased lead exposure and absorption.

When you have less time to get rid of lead, if there is any break in technique in protection, you will immediately see the response in increased lead absorption. In the past 22 years, we have always been able to warn management and the men themselves of peaks of heavy lead absorption suggesting breaks in engineering technique. In the eight years from 1935 to 1944, and the five years from 1944 to 1950, there were no cases at all. (Figure 1) In all cases of actual disabling lead poisoning there has either been engineering breakdown or delayed repair of faulty engineering ventilation equipment or even carelessness of men in using the respirators.

Concurrently with the Medical Department's warnings gained from qualitative tests, the engineering protection has been in a process of steady improvement. This has included the installation of a very effective dust disposal system with a bag house used on the machines which give off the greatest amount of lead dust in addition to the cyclone system collecting lead dust at other points of its evolution. During the process of improving the engineering control, so as not to interfere with the necessary production, certain men have been equipped with respirators, both the regular face masks (Bureau

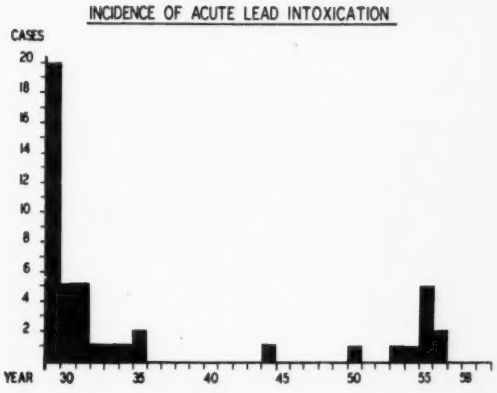

Figure 1

of Mines Approved) as well as positive pressure airline masks in certain cases. Current samples show that all are now under the safe limit of 2 mg per 10 cubic meters except one instance of 3.3 mg and one of 2.35 mg contrasting the high levels from 1944 to 1956 where air samples in seven instances varied from 7 mg to 23 mg. (Figure 3)

Over the past 28 years, the working environment has progressed from uncontrolled lead exposure in the totally unprotected work of hand mixing and hand pasting, on through the use of the early automatic machines which were not well exhausted, and finally up to the modern mixing, pasting and assembly, high-production machines where a great amount of engineering ventilation equipment has been built into the machines from the moment of their first design.

For 28 years we have had the opportunity to study clinically a slowly changing group of 50 to 100 men who have been exposed to the inhalation of lead in varying concentrations in storage battery manufacture. While there has been some change of personnel, our labor turnover has been very small, so that the majority of our men have been working in this same plant from five to 30 years. From the beginning, our work in the diagnosis of lead absorption has been based on the pioneering work of Aub, Fairhall, Minot, Reznikoff, and Alice Hamilton.[1]

In this series of cases we have depended chiefly upon the careful clinical examination of each worker at frequent intervals of from two to four weeks, depending upon the concentration of his lead exposure. The physicians have been trained in the general field of diagnostic medicine. This has included using the medical skills of history, physical examination including a search for lead line of the gums under a lens, (Figure I) observation of the blood pressure and the strength of the extensor muscles, as well as laboratory studies including hemoglobin, number of stippled red cells per 50 high power oil immersion fields, a routine urine and qualitative tests of urine for coproporphyrin.

Figure 2

In various learned circles, I have been somewhat shocked when physicians have said that there may not be any such thing as a lead line simply because they have never seen it. If you will look at the upper left incisor area in Figure 2, the left central incisor, opposite the base of the tooth, you will see the "lead" line. In the gum, not on the teeth, there is a row of dots or striate marks which means a deposit probably of lead sulphide in the gums. This will not wash off, and it will only disappear when there is a reduced amount of concentration of lead within the organism.

I know in the past that Dr. Aub used to have his residents take a small section of this gum line and look at it under the microscope, then one can see a black deposit directly under the mucosa. So here is the famous "lead line" that was described over 100 years ago before the Royal Society, and known since as the Burtonian line. Incidentally, all of those cases were cases where lead salts had been used as internal medication, nonoccupationally, in the treatment of patients in the hospital at that time.

We have changed our therapy somewhat and do not prescribe lead internally any more, but the lead line from occupational exposure exists as described originally by Dr. Burton. I spent a little time on that because there has been some argument as to whether there is such a thing as a lead line.

In addition to the clinical examination of the

patient and the base-line laboratory studies listed above, there has been clinical evaluation of the workplace in regard to lead dust inhalation in the storage battery plant by the same physician. This involves study and correlation of the worker's actual operations on his job, together with the physician's knowledge of his general physical condition and personal habits, along with a medical evaluation of the level of his lead absorption. Whenever a man showed danger signals indicating the probability of an impending disabling lead intoxication, he was either moved or given a positive pressure airline respirator while engineering protection was being installed or improved. In 1956, in two cases of threatened acute lead intoxication, expected time off from work owing to lead poisoning therapy was reduced from a period of several weeks to a few days by a course of intravenous Calcium EDTA under a hospital regime as described elsewhere.[2] No oral Calcium EDTA has ever been given to workers in this plant.

Years ago, collection of 24 hour urines for quantitative lead determination was done every few months to supplement the repeated clinical examination and the simple qualitative tests which were performed every two weeks. This was carried out for 15 years, from 1932 to 1947. However, it was found that the information gained by this more refined test of quantitative lead in the urine was of no more practical value than the simpler tests. In fact, it did not appear as helpful in our personal study of the individual worker as did the original tests of lead line of gums, strength of wrists, hemoglobin, stippled cell count and, later, urine for porphyrin. Though the Medical Department had often been urged to substitute quantitative studies of the urine for lead as a screening test in place of the lead line and stippled cell study, we became convinced that quantitative lead in the urine study *alone* was not safe. Therefore, study of the lead line, hemoglobin and stippled cell counts was continued throughout the entire 28 years of chiefly medical control of lead absorption in the worker. Routine examination of urine for qualitative test for coproporphyrinuria has also been done for the past nine years as a helpful adjunct leading to a diagnosis of lead absorption. We still believe it has basic implications in the metabolism of lead.[3,4,5,6] A number of authors and clinical workers in the field have noted that qualitative porphyrin tests are of distinct value in suggesting lead absorption becoming positive before stippled cells appear.[7,8,9,10]

Recently this whole question of lead absorption and intoxication has been here reevaluated as measured by both qualitative and quantitative laboratory determinations. This intensive study involved 15 men, two of whom had worked for three years, five for six years, two for 11 to 12 years and six from 20 to 32 years. They had all been exposed to heavy lead inhalation from time to time. It was already known that they had definite evidence of lead absorption because of the simple though frequent serial study of history, physical examination and qualitative blood and urine studies. Three men now have faint but definite lead lines and the majority have had on occasion stippled cell counts of from 10 to 25 per 50 oil immersion fields. These 15 men were chosen before there was any knowledge of their exact blood or urine quantitative values for lead. The clinical and qualitative tests alone had already shown that lead absorption was quite high and that these particular men needed to be watched closely. (Figure 3)

You will see on the left the column for qualitative tests, and on the right those for quantitative tests.

In regard to lead exposure, as seen by air analyses, the last column of figures on the right represents the average exposure covering a period of air analyses from 1944 to 1956. I am sure that you will see there have been some fairly high levels. This is the amount of lead in the air per 10 cubic meters, and if you wish to reduce its values per one cubic meter, just move the decimal point to the left.

The column next to the last on the right is the most recent air analysis, and you will see it has dropped sharply. This was done in 1958. However, in two instances, we are still slightly over the level of the permitted level of 2.0 mg per 10 cubic meters, namely, 3.3 mg and 2.35 mg.

These cases, as I have said before, are arranged according to decreasing concentration of lead in the urine. That is perhaps the most important correlation. I would like to point out that, in these 15 cases where we were trying to see if the quantitative lead gave us any information which the qualitative tests did not give, such information is noted in only one case, number eight. This was a man who was once heavily exposed to this concentration of well over 21 mg, though now only 3.3 mg per 10 cubic meters of air. He was using an airline respirator most of the time. There were certain periods when he had to take it off for machine repairs. He never showed a lead line. He, incidentally, is the man that has worked 32 years and is now "in the pink" physically.

He had only four stippled cells and his hemoglobin was 80%, or 12.6 gm, and he nearly always has had a 4 plus porphyrin test in the urine.

You see, in all instances except one, that those

LEAD ABSORPTION

	Clinical and Qualitative Tests - 1958						Quantitative Tests - 1958				
Case	Pb Line Gums	Stipple Cells 50/Hpf.	Hemoglobin Gms. %	Hct %	Porphyrin Plus	Porphyrin Micrograms 24/hr.	Pb Urine Mg/L*	Pb Blood Mg/100cc	Pb Air Mg/10cu m	Pb Air Av. 1946-1956 incl.
1	False	7	12.3 79	43	4	2380	0.39	0.115	2.35	7.59
2	1+	14	13.6 86	42	4	480	0.37	0.110	1.4	23.56
3	False	15	10.3 66	36	2	645	0.36	0.095	0.55	7.81
4	2+	10	13.5 86	42	3	1305	0.31	0.103	0.85	1.22
5	False	7	9.8 62	34	3	2055	0.31	0.075	0.55	8.56
6	0	12	11.4 73	41	3	180	0.30	0.081	0.6	0.84
7	0	17	11.3 73	39	4	825	0.26	0.097	1.27	3.62
8	0	4	12.6 80	44	4	1066	0.26	0.086	3.30	21.07
9	0	10	12.4 79	43	3	945	0.26	0.118	3.30	21.07
10	False	14	12.4 79	40	3	248	0.26	0.099	0.22	2.46
11	0	7	12.7 82	42	4	2100	0.24	0.099	0.97	3.31
12	0	6	12.7 82	45	4	1290	0.19	0.128	0.55	2.93
13	0	20	12.7 82	41	3	885	0.17	0.095	1.41	3.84
14	2+	23	11.9 76	39	4	2325	0.14	0.062	0.55	2.93
15	0	8	13.7 87	44	3	1020	0.12	0.102	0.94	7.39

*Adjusted to mean specific gravity (1.024)

Figure 3

LEAD ABSORPTION -- 15 cases -- Clinical Findings

Case	Occupation	Years Worked	Symptoms	Blood Pressure On hire	Blood Pressure Present	Urine, Albumin & Microscopic	Total Serum Protein*	Recommendation
1	A. Group	11	0	142/100	120/80	Negative	7.23	Give Pos. Res.
2	P. Salvage	6	0	140/90	130/90	Negative	7.23	Watch Res.
3	P. Inspec.	6	1956 Colic	140/90	122/82	Negative	6.85	Move & Iron
4	A. Dry chg.	12	0	130/90	130/80	Negative	7.23	Ventilation
5	P. Inspec.	6	0	120/80	130/80	Negative	7.23	Move & Iron
6	Cast Inspec.	3	0	140/90	120/80	Negative	8.04	Give Resp.
7	C. Winkle	25	0	112/70	120/80	Negative	6.68	Watch Res.
8	P. Oper.	32	0	125/70	120/80	Negative	6.68	Watch Res.
9	P. Oper.	23	0	120/70	110/80	Negative	7.42	Watch Res.
10	C. Pc	28	0	140/90	120/100	Negative	6.34	Watch Res.
11	M. Cycle	30	0	100/70	102/60	Negative	7.04	Watch
12	C. Auto.	6	1956 Colic	110/70	120/80	Negative	6.08	Ventilation
13	A. Sheet	3	0	122/72	112/80	Negative	6.85	Watch Res.
14	C. Auto	24	0	120/70	120/80	Negative	7.04	Ventilation
15	A. Racker	6	0	114/72	124/82	Negative	6.85	O.K.

*Normal range 6-8 gms.

Figure 4

cases show a three to four plus porphyrin.

In this case, number eight, the lead line level in the urine is .26 and in the blood .086. This is over the so-called safe level of lead in the urine of .15; but the blood is not much over the so-called upper limits of the normal of .07. Many have said that if we have a reading of lead in the urine of over .2, that is a level compatible with a coexistent state of lead intoxication. However, such a urine lead level certainly of itself is not diagnostic of lead poisoning. Some of these urine values run quite high; even as high as .39. Also, the blood leads in many instances run high, but the men show no symptoms.

Now I would like to point out case 14 to balance case eight. In case eight, we had very little evidence by qualitative tests of heavy lead absorption. In case 14, there was the safe limit of lead in the urine, .14, and in the blood .06, but on qualitative tests he had a two plus lead line, 23 stippled cells, with 76% hemoglobin, and a four plus porphyrin. Here the qualitative tests score over the quantitative tests. This man had never been sick and has worked over 25 years.

In Figure 3, his highest lead exposure was 2.9, but more recently only .055. He is working in charge of automatic casting where ordinarily we think there is very little exposure. We know that when the lead oxide contaminated scrap parts come over from the pasting line, they are dumped on a belt and go back into the pot.

We have had suction at the point of dumping, but are now placing suction around the conveyor belt itself.

There was no clinical evidence that serious, irreversible damage had been done to these men by this degree of lead absorption. If it had been felt that transient periods of increased lead absorption were likely to cause serious organic damage with residuals, we would not have relied entirely on the more easily available tests which are a measure of the individual's body reaction to lead. We wished especially to determine whether evidence of impending lead intoxication could be more sharply predicted by quantitative tests of urine and blood lead, rather than by the more easily obtainable tests that we had been using for many years.

What does this recent work on a small group of lead absorption cases from the storage battery industry show as regards the use of qualitative tests contrasting the use of complicated quantitative tests used in a search for early cases of significant lead absorption? By significant is meant cases where disabling lead intoxication is likely to occur in one to three months if no immediate effort is made to reduce the lead exposure. This can be done either by moving the worker or by insistence on the use of appropriate respirators while defects in mechanical protective equipment are being corrected.

In 13 of 15 men there was evidence of heavy lead absorption by both types of tests. In only one case (number eight in Figure 3) the simple qualitative tests erred in showing only minimal evidence of lead absorption by stippled cell and porphyrin though the quantitative tests showed definite though moderate indications of fairly heavy lead absorption. This is the case where the air concentration has frequently been over the safe limits of 2 mg per 10 cubic meters of air. The operator is a rather conscientious user of the positive pressure respirator supplied him. Not long ago his lead exposure shown by air samples was as high as 21 mg per 10 cubic meters, about seven times the recent reading of 3.3. This man had worked first as a hand mixer and then as a pasting machine operator for 32 years. At no time has he ever had even minimal symptoms suggestive of a possible lead intoxication, but we have watched him closely and recommended improvements in his engineering protection.

The quantitative tests erred in one case (number 14, Figure 3) by showing normal limits of lead in urine and blood while the qualitative tests warned of dangerous lead absorption shown by lead line, stippled cell and coproporphyrin in the urine as well as a moderate secondary anemia.

This individual has never been ill, though he has worked in this storage battery plant 24 years. Much improved engineering protection has been given him and more is planned.

Aside from these two cases, the remaining 13 showed that the individuals had potentially dangerous levels of lead absorption as measured by both qualitative and quantitative studies of lead in urine and blood.

The advantages and disadvantages of the two types of tests may be analyzed as follows:

I. The advantages of the clinical and qualitative tests.

A. Practicability, with the necessity of drawing only a few drops of blood and with only a very small amount of time demanded of the men away from their work.

B. Speed of determination is noteworthy, taking only 15 minutes in case of each stippled cell count.

C. There is no likelihood of lead contamination.

D. This method measures both lead absorption and intoxication in individual cases.

II. The chief disadvantage of the clinical and qualitative tests is that theoretically they are not "specific" for lead.

A. The lead line is indistinguishable from a bismuth line which formerly was quite common when bismuth was used for the treatment of syphilis. At the present time penicillin therapy has replaced the use of bismuth. The theoretical possibilities of a lead line being confused with mercury, thallium or silver is very unlikely because of the character and rarity of such findings particularly in a known lead worker.

B. Stippled cells are not specific because they may be found with any severe anemia with a low hemoglobin due to carcinoma, Hodgkin's disease or leukemia. In lead intoxication, however, stippled cells are usually plentiful with a normal or very slight reduction in hemoglobin. As Cabot pointed out in 1911, the finding of many stippled cells with a relatively slight drop in hemoglobin is characteristic of lead intoxication. It is not our belief that any one spot count of stippled cells is diagnostic. With three or four stippled cells we hire men as within normal limits. When studying a lead worker, if his stippled cell count rises quite rapidly within a few days from a base-line of six to 10 up to 15 or 20 or over, one can predict that there has been a breakdown of engineering protection such as with a blocked exhaust pipe or cracked lead pot. If the stippled cell curve continues to rise sharply when checked every two or five days, the man can be moved before lead intoxication occurs.

C. Coproporphyrins in the urine may be markedly positive due to other intoxicants such as alcohol and barbiturates, but in the known lead worker its finding in a frank four plus cerise color is most likely to indicate coproporphyrinuria from lead absorption.

III. The advantages of the quantitative tests are:

A. They can be done entirely by nonmedical and nontechnical personnel.

B. They can give a relatively rapid screening report on the level of lead absorption in a large number of workers — 100 or over.

C. These tests are truly specific only for lead.

IV. Disadvantages of relying entirely on the quantitative tests are:

A. There is the possibility of contamination in collection of urine and blood samples, as well as the objection of the men themselves to obtaining adequate overnight urines or a large 10 cc blood sample from the vein instead of a few drops from the ear. Even the advocates of the quantitative study of blood and the urine warn of the danger of lead contamination of such samples.[12]

B. There is paucity of clinical laboratories equipped to give accurate reports from quantitative studies of very minute quantities of lead found in blood or urine.

C. These tests measure lead absorption only and do not make a diagnosis of lead intoxication. They do not show the effect of lead on a given individual.

Comment

Determination of stippled cells in cases of lead absorption and lead intoxication is still of great significance. Besides our own experience, this is borne out by published papers of other men with experience in this field.[13,14] In whatever manner lead absorption is diagnosed and apart from the usually transient three types of lead intoxication listed below, the question arises as to whether lead absorption per se has done any irreversible damage to the organism. Aside from lead colic, with or without anemia, which occurs in 90% of the cases as the commonest type of lead intoxication from which the patient usually recovers without residual, there are the rare 5% or 6% of cases with lead palsies. Though these may occasionally show residual, such complications are rare if properly treated over an expected healing period of three months to three years. In the very rare instances of lead encephalopathy occurring in adult workers in modern industry, if the patient recovers there are usually no sequelae.[15]

The search for hidden residuals of lead absorp-

tion, should go forward. For example, there may be a transient, nondisabling secondary anemia as shown here in two cases of the 15 cases presented in this study (numbers three and five, Figure 3). They are being given iron and will be moved temporarily from further heavy lead exposure. We are also constantly searching for possible objective evidence of any permanent injury from chronic lead absorption.

Figure 4 shows the years worked and the symptoms and blood pressure for comparison with the time when the men were hired many years ago, and now within the last month. In only one case was there a rise in blood pressure and that not too much.

This correlates with the report that we made previously on blood pressure in workers in the lead industry studied over a five-year time, and also with the report and comments by Dr. Mayers and Dr. Hamilton as to the fact that there does not seem to be any definite correlation between long, continued lead absorption and an increase in blood pressure.

The routine urines studied for microscopic findings and albumin were all negative, and in addition, the total serum proteins were all within normal range.

In our own experience and knowledge of the literature, we are led to believe that mere lead absorption without the symptoms of lead palsy or encephalopathy causes no permanent physical harm to the adult human. Further, apart from those rare cases of colic with short periods of acute disability, there is no increase in plant absenteeism or loss of work ability in our experience. There is also no weight loss, no consistent blood pressure abnormality and no damage to the kidney as measured by routine urine analysis, while one sees no evidence of liver damage either in the form of jaundice or in the estimation of total protein. (Figure 4)

We would welcome reports of cases of other workers in the field where the qualitative tests mentioned above are followed out routinely and in detail by a physician together with the more complex quantitative tests of lead absorption.

Conclusions

1. Together with clinical examination and evaluation by a physician, the qualitative tests of stippled cell, hemoglobin and urine porphyrin have proved effective in estimating levels of lead absorption. This is true in the majority of lead-exposed workers observed in this storage battery plant in the last 28 years, and in 14 out of the 15 cases discussed in this paper.

2. These qualitative tests have never failed to warn of heavy lead absorption in time for moving or otherwise protecting the men, except in the rare instance where management or worker have been unable to cooperate immediately in the recommendations of the medical department.

3. Quantitative examination of the urine for lead is a useful supplementary aid in evaluating lead absorption in those instances where large industry is financially able to support this complicated and somewhat difficult test.

4. Blood lead tests, though requiring great care both in avoidance of contamination and in complicated chemical manipulation, are of great value for medical-legal and research problems. They have not seemed practical for the routine study of the individual with lead absorption in the average lead storage battery plant.

5. Qualitative and quantitative blood or urine tests for lead are not of themselves diagnostic of lead intoxication. They are merely signs of lead absorption to be judged by the physician in the light of the whole clinical picture.

6. Frequent clinical examinations of worker and workplace by the same medical observer, together with qualitative studies of blood for hemoglobin and stippled cells examined serially every few days, as well as occasional urine porphyrin tests, are of most practical help to a physician experienced in the clinical control of health in the storage battery industry.

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DISCUSSION

MR. WILLIAM M. PALLIES: I think one of the big problems we have here is defining lead intoxication, and as far as I can see from a workmen's compensation point of view, things are gradually changing and the social climate has brought more and more things under the workmen's compensation laws.

I think we will have more and more of these little illnesses which have occurred and have been passed off before, which will now be called lead intoxication. So my contention is that we must set limits on urine and blood leads, and then say that as far as we can see, if anybody exceeds these, there may be trouble; the man is going to develop lead intoxication or he is going to have a good legal claim. If we have the evidence of urine and blood leads which exceed what we consider dangerous levels, then the Industrial Commission is going to consider that the man has lead intoxication.

To me, Figure 3 demonstrates very clearly something which I have held all along. When you examine the blood lead levels, with few exceptions they are all in excess of .08 mg per 100 gm of blood, which we have always considered to be a dangerous level, and these men should all be removed from exposure to lead except possibly number 14.

I don't understand number 14. He has a lead line. He has four plus porphyrin, but he certainly isn't showing any great lead exposure as far as blood urine lead levels are concerned. Other than that case, the urines, the bloods, the porphyrins and possibly the low hemoglobins indicate that these men have been exposed or are being exposed to too much lead. So I would substantiate a case from this figure for the quantitative studies.

DR. PAUL REZNIKOFF: It would be a grave mistake if we made any diagnosis of lead poisoning on the basis of the amount of lead in the urine or blood. If we try to make our diagnosis on the basis of what we think compensation boards or industrial medical boards might say, we would not be making our diagnosis on a medical basis.

I agree with Dr. Belknap and the industrial hygienists who say that the actual quantity of lead in the atmosphere, of lead in the blood, of lead in the urine are all guides, but the diagnosis of lead poisoning should be based on disability due to lead, and not on chemical findings.

Naturally it is common sense to suppose that the more lead you have in the blood and the urine, the greater rate of disability you will have, but that doesn't make the diagnosis in the individual case.

MR. PALLIES: Being an industrial hygienist, I am not interested in diagnosing lead intoxication. What I am trying to do is minimize the exposure, and I have depended on the medical authorities to set certain limits which have worked out pretty well for us in the electric storage company.

When we have kept lead levels below about .2 in urine and .08 in blood, we have had no trouble whatsoever. So we really have had no lead intoxication to diagnose.

DR. R. A. KEHOE: I do not intend to enter into a discussion, or to express a difference of opinion with reference to the diagnosis of lead poisoning. I think it may be said, once and for all, that the diagnosis of lead poisoning is made only where actual illness exists, and then only by clinical means. If the individual is ill in any way that can be demonstrated on the faintest evidence or the greatest, we may then make a diagnosis of lead poisoning. I call attention to the fact that every man in the group represented by Dr. Belknap's figure had a four plus porphyrin. I don't know precisely what that means, because its significance is related to the nature and the precision of the test that was carried out. Moreover, this test is nonspecific, with respect to its relation to lead as the cause of the abnormality, as are all the other so-called nonquantitative findings. Nevertheless, the appearance of abnormal quantities of porphyrins in the urine, if they can be attributed to lead and lead absorption, are, I believe, the first sign of the existence of lead intoxication.

Whether it is followed by severe disabling illness is another matter, and we do, I think, have to recognize that there are men who do not develop palsy or encephalopathy or colic, but do develop hematologic signs of lead intoxication.

There are many other things that could be said, but I think it should be said that this abnormal finding indicates quite clearly that the industrial hygiene in this lead storage battery manufacturing industry, if this were a representative illustration of it, is not yet good enough. What we are talking about when we apply standards of analytical precision to the blood and urine is not the diagnosis of lead poisoning, but the recognition of the existence of danger, and there are adequate experimental and observational data that demonstrate quite clearly the relationship, the correlation, between the analytical findings (if you can determine the level of lead excretion by the analysis of a sufficient number of samples, or if you can measure the general level of the lead absorption in the body by means of analyses of the blood), and the degree of danger associated with the occupational exposure.

Thus, we may say that an individual is not in danger if the analytical values are below a certain point; we may also say that the danger increases, the danger of the occurrence of intoxication and the degree of its severity will increase as these values range upward above certain critical levels. This is, therefore, not a question of diagnosis. It is a question of the measure of danger, and I must insist, as I have through the years, that when we have achieved such a quality of industrial hygiene in the lead trades that enables men to work without danger, we have done a good job. Until we have done that, we have not done enough.

DR. J. H. FOULGER: I agree with the discussion leader. The function of the physician in industry is to prevent. Diagnosis is an indication that we have failed. Prevention is a far more difficult thing than diagnosis, and in prevention we are virtually trying to discover whether a crime is being committed, not has been committed; and all the evidence we can get, qualitative or quantitative, which, when added together, shows that a crime is being committed, is what we need.

In view of what Dr. Reznikoff said about the porphyrins, there is another very interesting observation in another field of medical science. Recently Borsock of Cal Tech, in studying the incorporation of amino acids into proteins, found that the incorporation of amino acids into reticulocytes is greatly hindered by many compounds of which the most active is lead, that a molecular concentration which corresponds to the level in the blood of lead, which we look upon as a sort of borderline between a serious lead hazard and one that we can ignore, is a level at which lead in Borsock's experiments prevented incorporation of amino acids into reticulocytes, and therefore, the metabolism of hemoglobin.

MR. PALLIES: I was very happy to see these results, especially on porphyrins. I have been asked many times about what to do, in a small plant where 20 or 30 people are exposed to lead. A complete laboratory set up to do urine and blood leads is out of the question. Yet, something must be done. In such a situation I recommend urine porphyrin analysis.

I think Dr. Belknap's work on these 15 men demonstrates the value of porphyrin analysis, and apparently he is backed up by some of the people here today.

DR. BELKNAP: I would simply say in closing this discussion, that I have made no claims to indicate that ours is a perfect situation as yet, but I think you will see I have pulled no punches. I have given you the facts on what high levels of lead absorption we have, and it is obvious that we should aim to reduce them.

However, in this plant, as in the majority of middle size to small battery plants, where they have no access to reliable urine or blood lead determinations, I have given you something of a yardstick for lead absorption. I believe this will hold in keeping people clinically well while we are reducing the lead exposure.

As Dr. Reznikoff said, the diagnosis of lead poisoning finally is a medical problem, and in our part of the country the Industrial Commission boards place great weight on the decision of the physician as to whether a patient is really suffering from lead intoxication, or whether he has other coexistent illnesses.

They usually pay compensation as yet only for disabling lead intoxication. It is quite obvious the flood of claims which might develop in certain areas of the country should one go to the point of attempting to make a diagnosis of clinical lead intoxication directly or indirectly by quantitative laboratory tests alone.

I believe that such quantitative tests are valuable in helping point out danger spots, but I expect to continue to use our periodic qualitative or nonspecific tests, and at the same time attempt to reduce the level of lead exposure.

A-U-T-O-M-A-T-I-O-N

In the field of industrial medicine, I believe that with increasing automation the problems produced will be due not so much to the nature of industrial life as to factors in non-industrial life which directly affect the efficiency of a worker for his industrial life. We know that this situation already exists in the chemical industry. The out-of-industry activities of our workers can very seriously affect their ability to withstand the hazards to which they might be exposed in the plant. Increased spare time will intensify this situation. It may produce a very complicated picture if that spare time be used in activities which lead to great fatigue, physical injury, or physical deterioration. This is the real problem we face in the future from automation.

The conversion of workers from jobs which require a certain degree of physical labor and allow the worker to see to some extent what happens as the result of that labor to jobs which require merely the reading of dials and "push button control" should the readings reach a danger area, involves many problems of psychology. In solving these problems, the total life of the worker and particularly the stresses to which he is subjected in his family and social life away from industry can be of the utmost importance.

We may, therefore, expect that the era of automation will demand more attention by industrial nurses and industrial physicians to the whole life of our workers. It will require more careful selection of workers both from physiological and psychological aspects so that they may be properly allocated in industry.

—John Foulger, M.D., in *AAIN Journal*, August, 1958.

HEALTH CONTROL in the CERAMIC INDUSTRY

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To a considerable extent, our report is designed to demonstrate an approach to a lead control problem that has been successful and may contain suggestions for industrial health workers faced with the same problem in the future.

We manufacture several hundred glass formulae for use as protective and decorative coatings for metal and clay. We are the world's largest supplier of these products, but when compared to the total glass and ceramic industries, we represent only a small, specialized portion.

Our operations demonstrate a lead exposure problem less significant than that of other industries using lead because lead in glass complexes presents a different degree of solubility than in other forms. We also demonstrate the importance of recognizing that solubility is increased as the particle size decreases and presents more surface area for chemical action.

Our fritted glasses, porcelain enamel for metal and glaze for clay bodies, range from the simple lead borates to lead-sodium-aluminum-potassium-calcium-boro-silicates. The lead content varies from 2% or 3% to 70%. Our glasses have unique characteristics among which is to resist attack from certain types of exposure. The best known is an acid resisting glass. Our glasses mature or fire onto metal or clay at temperatures ranging from 980° F to 2500° F. The metal coatings require a relatively short exposure to maturing temperatures, sometimes a matter of a few seconds. The glaze coatings for clay bodies must be designed to mature with several hours exposure at higher temperatures.

At present, only a few of our production items contain lead. One plant uses up to 80,000 pounds of litharge per week compared with the weekly production of 870,300 pounds of glass. The average is less than 10% of the number of production items containing lead.

One part of our industry effectively demonstrates a singular lack of lead phobia. The pottery industry is changing from raw glazes to fritted glazes which provide lead, where essential, in a less soluble form.

The Great Britain "Pottery Act," which is now more than ten years old, reads, "Use lead (and some other toxic materials) properly and you should experience no trouble. To help you, our agency has much experience and this should be applied to your process."

My personal introduction to the lead problem occurred with my assignment as Safety Director of Ferro Corporation about ten years ago. As any safety engineer will do when accepting a new assignment, I surveyed the problems contained within that assignment and I identified the problems that should have the priority of attention and work. My survey was not completed before an employee began showing symptoms of acute lead intoxication.

Following the then prevalent practice in industry with lead exposures, we screened all employees in our plant and laboratories with the stippled cell count technique. To assist our Medical Director, Dr. W. W. Markley, all available literature was reviewed. At that time, the literature contained almost no references to the solubility of lead glass compounds. We did find data relating to the coproporphyrin presence in urine in lead exposures. The deLang and TenBerg test was immediately added to our battery of screening tests. The initial results were very encouraging. A qualified medical technician was employed to continue the work of testing each exposed employee each month with the porphyrin check and the stippled cell check.

The results showed acceptable correlation. The conservative medical judgment that had to be applied indicated the desirability of more exten-

sive laboratory work. Acting on this judgment. management provided a completely equipped laboratory and authorized the employment of a biochemist.

Several meetings were held involving plant supervision, plant employees and the officers of our union. The purpose of these meetings was to acquaint the men with our goals and the methods elected to reach them. The meetings contained an admission of our inexperience and a guarantee that the entire program would be conducted in the open.

Ten years ago, this approach to a problem of this type was discouraged by some lead industries. Looking back, we have never had any reason to regret our action. Today our plant and laboratory personnel have full access to their lead report records and as a result of the indoctrination and training, frequently help us pinpoint their lapses in working techniques that produce slight elevations in lead signs. They demonstrate no lead phobia. We have had no cases of lead intoxication.

We can report only two or three situations in 10 years wherein the family doctor of one of our employees with vague gastric disturbances found it necessary to make a tentative diagnosis of lead poisoning, the familiar difficulty of lead industries' medical departments.

Our effective control measures now include: (1) Two changes of clothing per week. (2) Regular bathing from daily to biweekly depending on job assignment. (3) No smoking and eating without prior washing of face and hands. (4) Smoking and eating prohibitions in production areas. (5) Daily issue of a clean respirator. Each employee is assigned two. Only three areas are "respirator areas," yet a number of employees voluntarily use respirators in other areas. We encourage this because our glasses contain silicon, chrome, zirconium, antimony, potassium, copper, manganese, nickle, boron, strontium and cadmium, to name a few. (6) Dual lockers; one for street clothing and one for work clothing.

Our laboratory work included comparisons of quantitative and qualitative porphyrin findings in the urine with blood leads, urinary leads, and stippled cell counts.

We believe the porphyrin check provided a better lead screening examination than could be obtained by examining blood smears. We estimated 13% greater accuracy. We were faced with an occasional negative blood smear which was not supported by a negative porphyrin. In addition, the laboratory conclusively demonstrated the value of the following points: (1) The specimens were more cheerfully given by the employees. (2) Time and trouble to obtain and process the specimens were greatly reduced. (3) We included, and still do, a porphyrin examination on the pre-employment urine specimen which is a part of our complete clinical examination.

This side light is interesting because we started the practice in an effort to provide a type of control for our work. Our medical department has continued the practice because a positive porphyrin in any degree, as a part of the pre-employment physical examination, should be checked out. It is a sign something is wrong. Briefly, our checking out has revealed a few cases of uncontrolled pre-occupational exposure to lead, some rather significant respiratory conditions and two documented carcinomas.

This type of screening examination now has the approval of our State Department of Health. We use it in four plants and the new aluminum enameling industry shows a preference for the technique. In a few cases I have provided precise standards and taught lay plant employees to perform the test. We offset the question of lay evaluation of results by requiring medical supervision of all positive specimens.

Under normal circumstances, an employee will produce a negative porphyrin as a part of the pre-employment examination. From two to six weeks following his start to work in the lead exposure, he will demonstrate an elevated porphyrin, usually of the plus one or plus two variety. Within two to six weeks, the elevation disappears. We presume this is accounted for by the fact that his physiology is adjusted to the new environment and is operating so as to receive and discharge lead below the maximum permissible level. I will not dispute that new employee indoctrination produces a degree of adjustment in personal habits and hygiene which could produce the same results. Both points have value in teaching employees.

Each month we publish a graphic demonstration of the lead volume processed by the plant. We think this is important in our role of placing all the cards on the table. Early in our efforts to educate the employees, it was possible to trace certain lead production items, department by department, through the plant by screening test results. Today, with the engineering changes and improved employee education and attitude, it is no longer possible to do this. In fact, we now find it difficult to obtain a large enough group of employees with significant positive porphyrins from screening tests to obtain blood and urinary leads to make the necessary cross checks we think should be a part of a conservative attitude in our control program.

In our plant we test 300 employees per month. In general, trace and plus one positives are of the greatest interest to the employees, nurses and

the safety department as they may indicate individual or group trends. Plus two's are referred to the medical director and immediate supervisor. The supervisor reviews working techniques. The doctor's check includes weekly "porphyrin checks." Depending upon clinical findings, employees' history of sensitivity to lead, blood and urinary leads are ordered from two plus to four plus. One year produced so few three and four pluses that we enlarged the group to include two plus positives to obtain 15 or 20 blood and urinary leads as checks per year for control. Employee job changes out of lead exposure areas are usually only necessary in the four plus range and then if the employee has two consecutive weekly checks producing four plus.

I believe that the published maximum allowable concentration of 20 milligrams per cubic meter of air should be revised to provide a suggested allowable concentration for each lead compound. Our lead compounds range from 3% to 70% elemental lead and we have obtained air values up to 60 milligrams of lead per cubic meter with the employees showing zero elevation in lead absorption signs.

In our case, the probability of the plant working on one lead compound exclusively long enough to obtain samples is remote. We usually have several adjacent smelters or grinding operations processing a separate lead compound. Lead glass complexes obey the laws of temperature elevation, i.e., elevated temperatures will produce lead vapors where degree of vaporization is also related to the chemical composition of the glass. Certain glass complexes chemically bind the component raw materials into higher stability. Our technical staff suggests that high alumina has this property.

Other technical personnel have offered the suggestion that the higher the valence, the greater or higher the toxicity. Apparently this approach to various industrial toxicity problems needs more study and consideration relating to several troublesome compounds.

Much worthwhile progress could be made by the lead producers if they would consider the problems they are trying to solve from a more practical point of view. I refer specifically to a recent attempt to reduce dust by pelletizing litharge. As I understand it, some of the pelletizing binders introduced undesirable properties into the finished glass. In one or two trial runs involving pelletized material, about one-half millimeter in diameter, the grinding action of the pellets enroute between a plant and our mixing department produced an unusually fine dust which gave us a heavier concentration of dust than we normally experience with untreated litharge. The size of the pellet may not be as important as recognition of the fact that litharge and many other lead compounds do not stay air-borne for more than a fraction of a second. One hundred mesh material is air-borne longer than 50 mesh material. Also, larger pellets will move in the batch as it is worked in our processing.

I heartily subscribe to the Health and Safety Division of the Lead Industries Association. Since learning of their operations approximately 10 years ago, we have had an opportunity to draw heavily on their advice and counsel. It is a sincere regret that there is not more staff and money to provide the services of the type they supply industry and the public.

Lead compounds provide a more useful glass. Our industry is interested in new markets. I am convinced some new products and markets will require new properties in our product. There is no reason to avoid the use of lead to reach these goals.

DISCUSSION

DR. C. H. HINE: I should like to reemphasize that the appearance of porphyrins in the urine is not solely diagnostic of lead intoxication since increased secretion of porphyrin precursors occurs in a number of diseases, most of which involve the liver or the blood, but which may also extend to include mental diseases, diseases of the skin and chronic infections of various types. There are, however, qualitative measures for distinguishing between coproporphyrin III, the derivative of most importance in this problem, and other closely related precursors of hemoglobin. Recently, Minden and Thiele (*Arch. f. Gewerbepath. u. Gewerbehyg.*, 16:396, 1958) demonstrated that the number of different urinary porphyrins, as demonstrated by paper chromatography, increases with the increased absorption of lead. If and when more specific analyses are required, these can be accomplished. I do not believe at this time that a discussion of the exact mechanism of the formation of these materials is relevant, since despite considerable research work there are many facts still to be elucidated. However, suffice it to say that as a screening procedure, there is a high degree of correlation between the results of elevation in these coproporphyrin values and urinary and blood lead levels. This test is used with increasing frequency today. Its value was recognized by us some 10 years ago, and we have since instructed our medical students at the University of California in its use as an index of lead absorption. It is my understanding that a number of industries use the procedure rather widely.

The relatively large particle size of the glass frits and the chemical structure of lead with its incorporation as a borate and silicate all mitigate against absorption into the body. Despite these factors, it would be my recommendation that serious consideration should not be given to altering the present threshold limit values of 0.15 mgm/M^3, principally on the basis that it would complicate the present

analysis, since determinations would be required to indicate the relative percentages of the molecular forms of the different lead compounds. Mr. Frank's studies have, however, contributed further to the understanding of lead hazards since he has pointed out that air concentrations of lead silicate and borate considerably above threshold limits, when compared with determination of lead excretion patterns and the physical status of employees, have failed to demonstrate any evidence of either frank or subclinical intoxication.

In addition to the responsibility in the field of health protection for its own employees, management has the responsibility for safety of its product under conditions of ordinary use. As Mr. Frank has indicated, ceramic products may contain considerable quantities of lead, and on occasion they have uses which bring them into contact with the preparation or serving of food. It is my understanding that the industry has voluntarily accepted a standard of the quantity of free lead which can be expected to be extracted from container surfaces. In this regard I would like to refer to some experience we had on the West Coast with the import of some improperly glazed and painted dishes from Japan. Analysis showed that the glaze could contain as high as 32% extractable lead, and this was deemed to be a public health problem since it was felt that continued use of dishes with unstable linings could result in ingestion by consumers of enough lead over a period of time to result in illness. This problem has been corrected without any serious mass intoxication. I am sure that due to the efforts of the Health and Safety Division of the Lead Industries Association such problems are avoided in American industry.

MR. FRANK: I want to say just one thing for our industry. Lead compounds give us more useful glass. Our industry is interested in new markets, and I am convinced that new products are going to require new properties which can be obtained from lead. I have no reason to avoid the use of lead to reach these goals.

DR. HINE: Is the problem of lead intoxication in children still met quite frequently in the Boston area and the East? We don't see it very often in California.

DR. R. K. BYERS: Our lead poisoning is mostly in children who chew paint on the cheap housing that was put up in the 1870's, 80's and 90's. Much of this is painted with lead pigments on inside trim. At our particular hospital, we see anywhere from two to 15 cases of lead intoxication annually. Very few of them come from any other source. We have an occasional case of a child from the country where an old-fashioned lead containing ointment has been applied to the mother's nipples or something of that sort, but practically all cases are from the very cheap housing of the period mentioned.

DR. HINE: Has anyone had any experience with intoxication from water from lead pipes, acute intoxication?

We believe that such a problem occurred when the water supply in the older part of San Francisco was moved. During that time, the lead content increased quite a bit in the water supply in one area, which we thought produced a hazard of lead intoxication. Has anyone else had experience with that?

DR. R. A. KEHOE: Cases in adults still continue from time to time, particularly in rural areas, when water is conveyed to a house from a spring or well in a system of lead pipes. We see cases of that kind from time to time, and then there are also occasional cases seen in new housing developments where the luting of water pipes with lead-containing luting material results, for a period, in a high lead content in the water.

These are rare, but there are in the literature at least two reports of virtual epidemics of this kind in large areas of new housing developments.

Rising Falling Sickness

Epilepsy is as common in the United States as diabetes or active tuberculosis and occurs four times more often than polio. At least one in every 200 Americans has this condition in mild or severe form, according to the current issue of *Patterns of Disease*. Estimates of the incidence of epilepsy range from 640,000 to 1,700,000 persons, but no precise estimate can be made since the epileptic person hesitates to reveal his affliction. Approximately 52,000 persons develop their first attack each year.

According to *Patterns*, existing Workmen Compensation laws do not encourage employers to hire epileptics. Ohio is the only state where the law provides for second-injury funds to pay benefits to employed, afflicted epileptics without requiring the employer to pay the compensation directly.

HYGIENIC LEAD STANDARDS

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The significance of hygienic standards depends as much on communication as it does on science and technology. The terms hygiene standard, maximum allowable or acceptable concentration, permissible limit, threshold limit and hygienic guides are used interchangeably. Individual interpretations of the figures are certainly not the same. This is partly owing to a lack of understanding of the technical aspects and the purpose of the standards, and partly to the fact that legal or regulatory connotations are inferred. The latter is a particular stumbling block as there is a tendency to use the standards to "prove" that an injury could or could not occur. Only when the purpose and limitations of the standards are thoroughly understood can they be properly utilized and the greatest benefits obtained.

Standards of good practice have been established in many fields. They are based on available scientific and technologic information and the judgment of a group with knowledge of the particular subject. It is obvious that each member of the group will not have initially the same numerical value in mind, and that the final standard must represent a compromise. The figure finally accepted will be a "round number" and not an "exact" figure. Standards must be recognized for what they are, the consensus of a group exercising its best judgment. The figure accepted is not a fixed scientific value, and might just as well have been somewhat smaller or larger.

The purpose of hygienic standards is to serve as guides in controlling the industrial environment to protect the health and comfort of workers. However, the final criterion of the effectiveness of the standard and environmental controls does not rest upon analytical environmental data, but upon the response or lack of response of the worker, which is determined by comprehensive and thorough medical surveillance. The closer the correlation between the environmental measurements and the results of medical examinations the more meaningful the hygienic standards.

There are three interrelated factors which govern the effective application of hygienic standards: (1) the limits of analytical measurements, (2) potential severity of the hazard and (3) reliability of diagnostic procedures.

The wide variations in the levels of air contaminants to which a worker may be exposed make it difficult to obtain an integrated measure of exposure with a reasonable number of samples. The evaluation of the hazard may be good or bad depending on such variations and the effects that peak concentrations may have on the worker. Hence, the hygienic standard may be more accurate than the analytical data obtained to evaluate it. This limitation of air analyses can be minimized by instituting engineering controls at sources of high contaminant dispersion, thus reducing peak concentrations. The close relationship between the standards and sampling and analysis is obvious.

A safety factor is an essential consideration in establishing a standard. The magnitude of the safety factor may vary greatly depending on our knowledge of the biological action of the substance in question. If the potential hazard is great, if the margin between minor injury and serious injury is narrow, if the injury produced is irreversible, then a greater margin of safety is required. On the other hand, if the margin between the incipient effects and serious injury is large, effects are readily reversible and good diagnostic procedures are available to detect early changes, then the margin of safety can be small. The type of biological action is also important; for example, whether the action is one of progressive systemic effects, narcosis or irritation. It is interesting to note that the present accepted standard of 1 ppm for chlorine and bromine is the same as given in a table published in 1912, whereas the values for solvents such as benzol and carbon tetrachloride have been greatly reduced.

It should be evident that a figure in a table of standards or limits has no significance per se, and does not define the relative hazard. It has meaning only when interpreted in terms of analyt-

ical, toxicological and medical data applicable to each individual compound. If the legal implications and use of limits to support otherwise untenable positions could be eliminated, the value of standards would be greatly enhanced and the establishment of acceptable standards would be much less difficult.

Standards relating to the concentration of lead in air, urine, blood, water and paints are discussed in the following sections.

Hygienic Standard for Lead in Air

Air analyses are specific measurements of the environment, and permit an evaluation of a hazard before workers are exposed. They have a definite advantage over other measurements which depend on some biological response of the worker to the exposure. Another important use of air analyses is the determination of the sources of dissemination, thus directing engineering control to those points where controls are needed and at the same time serving as a basis for selecting the type of control most desirable. Subsequent to the establishment of control measures, air analyses can be used to check the effectiveness of the engineering measures. Thus air analyses have a unique role in the prevention of harmful or objectionable effects from environmental contaminants.

The value of such analyses is meaningful, however, only when they can be interpreted in terms of potential hazard; hence the need for hygienic standards for the concentration of contaminants in the air. Briefly, hygienic standards for air concentrations are based on laboratory research using animals, and field studies correlating the medical observations of exposed persons with data on the concentration of contaminants to which they are exposed. Limited human experimentation in the laboratory and experience in the use of a standard serve to substantiate its validity or indicate a need for revision. The better the correlation between air concentration and effects, the greater the reliability of the standard.

It is unanimously agreed that the translation of the results of animal experiments in terms of human response has definite limitations. Hence a factor of safety is used and this may vary widely. A standard based on animal data alone is usually considered tentative. Standards based on field studies are, in general, more reliable. But owing to many factors, such as limitations of air analyses (wide fluctuations in concentrations, physical state of the contaminant and number of analyses usually obtained), lack of precise diagnostic procedures and the difficulty of estimating past exposures, these values also are established with due consideration to factors of safety. In other words, using the best tools available, hygienic standards for air concentrations are not highly accurate fixed values, but rather represent levels of magnitude.

Based on the results of an engineering and medical study conducted by the U. S. Public Health Service in a storage battery plant, it was concluded that "Except for prolonged exposure, it appears that the limit of safety under the conditions encountered in this study is an atmospheric concentration of lead dust or fumes of less than 0.15 milligrams per 10 cubic meters of air." Prior to this, a value of 0.5 mg/cu.m. had been used by some. Others were of the opinion that 0.15 was too low and that 0.3 mg/cu.m. was more realistic. Nevertheless, since the publication in 1933 of the storage battery report, the hygienic standard for lead has been generally accepted as 0.15 mg/cu.m. The fact that this standard has been used successfully for about 25 years indicates that it has been a reasonable value. This does not necessarily make it the best choice nor demonstrate that other values of the same general order of magnitude such as 0.1 or 0.2 might not have proved just as satisfactory. In fact, a standard of 0.2 mg/cu.m. has recently been adopted by ACGIH and the Hygienic Guides Committee of the American Industrial Hygiene Association.

The main compounds of lead encountered in the storage battery plant were: PbO, Pb_3O_4, PbO_2, and $Pb(SO_4)_2$, and therefore the figure 0.15, previously quoted, must refer to exposure to these materials. However, the figure is sometimes used to refer to "lead" in an all inclusive manner. The ASA standard is limited to lead and its inorganic compounds, carbonate, sulfate, oxides, nitrate and chloride. While it is impractical and unnecessary to establish individual standards for each lead compound, it is realistic to make distinction between soluble and insoluble compounds in establishing standards for systemic poisons. For example, two standards were established for uranium and vanadium compounds, one for soluble and another for insoluble compounds. This same principle should apply to lead compounds and is presently under consideration by a committee of the American Standards Association.

Another important factor in regard to air concentrations is particle size. The effective dose of lead is that portion which reaches the lungs and is absorbed into the blood stream. This is supplemented by the lead which is retained in the upper respiratory tract, removed by the action of the cilia, and swallowed. Since probably 90% of the swallowed lead is excreted unabsorbed, a large portion of the lead which enters the respiratory tract may not be absorbed if

the particle size is large, and the air concentration, which is determined in terms of weight, may exaggerate the exposure conditions. On the other hand, if all the particles are present as a finely divided fume, the effect may be somewhat underestimated.

It is not so much the standard which is finally established, but rather its proper use which is most important. The evaluation of the potential hazard of the environment should be only one facet of a well-balanced program, and should be correlated with engineering and medical control measures.

Hygienic Standards for Lead in Urine

In view of the limitations of air analyses and the fact that exposure to lead compounds has meaning only if lead absorption occurs, it was natural to turn to the analysis of biological materials to provide a measure of lead absorption. Numerous studies have provided much quantitative information on the relationship between urinary lead excretion and severity of exposure, and the analysis of urine specimens is probably the most common procedure for evaluating lead exposure and absorption.

Normal urinary lead excretion varies from about 0.01 mg to 0.08 mg per liter in large samples of a liter or more, and from 0.05 mg to 0.12 mg per liter in spot samples of 50 ml or more. The mean value is in the order of 0.03 mg per liter. Values of 0.15 mg and 0.20 mg per liter have been generally used as an upper safe limit for urinary lead excretion. However, concentrations considerably in excess of these levels have been found in the absence of any significant evidence of lead poisoning. Conversely, evidence of lead poisoning has occasionally been observed with concentrations less than 0.15 mg per liter. As there may be an overlap in the distribution curves of urinary lead levels in unexposed and exposed personnel, a single result has little meaning. Repeated analyses, noting trends, and the findings in a group of exposed persons reveal more meaningful information on the magnitude of the exposure. The higher the level above the normal range, the greater the likelihood that poisoning will occur, but there is no specific level above which it can be stated that poisoning exists. In other words, urinary lead analyses cannot in themselves be used to diagnose lead poisoning, but they are of value when used in conjunction with other data and clinical findings in the evaluation of the significance of the exposure and in the diagnosis of lead poisoning.

As mentioned previously, urine analyses may indicate a low level of absorption even though air concentrations may be high owing to large particle size or insolubility. The reverse of this also may occur. In one instance in which air analyses showed values well within acceptable limits, and the urine values were quite high, it was found that the exposure was from a source outside the plant. Thus the two procedures can be used to supplement each other in evaluating exposure to lead.

In summary, although a standard or limit value for lead has been established, in practice a sliding scale or range is more commonly used. For example, values below 0.1 mg per liter of urine may be considered of little or no significance, values between 0.1 mg and 0.2 mg constitute an intermediate zone, and increasing values above 0.2 mg are evidence of hazardous lead exposure and the need for improved engineering control. Used in this manner, in conjunction with environmental data and medical findings, there need be little controversy regarding a single standard for the concentration of lead in the urine.

Hygienic Standard for Lead in Blood

The concentration of lead in the blood also provides a helpful index of lead exposure and absorption. It also serves as an aid in the diagnoses of lead poisoning by providing definite evidence of lead absorption and is particularly valuable in cases of nonspecific symptomatology. Blood lead determinations have the advantage that the sample can be collected without the active cooperation of the individual, and without the risk of contamination. Blood lead concentrations are less variable than urine values, and in rare instances of kidney impairment reveal excessive absorption where urine analyses would fail to do so.

In general, however, the same principles apply to blood concentrations as to urine concentrations, namely, there is no specific level of blood lead which can be interpreted as indicating that lead poisoning exists. Blood lead concentrations of the order of 0.01 mg to 0.06 mg are considered within the normal range for persons with no industrial exposure to lead. Values between 0.06 mg and 0.08 mg may be considered a transition zone, and concentrations above 0.08 mg are indicative of unsafe exposure and that control measures should be improved even though no signs or symptoms or clinical evidence of lead poisoning are present. There may be a disagreement regarding the figures given; however, the principle of a sliding scale is certainly valid and as long as the values are used to evaluate exposure and absorption of lead there is no need to place undue significance on a specific figure.

Hygienic Standard for Lead in Drinking Water

The establishment of a hygienic standard for the lead content of drinking water presents a

somewhat different problem as the opportunity for control, monitoring and surveillance is not as readily applicable to the general public as it is to industrial workers. Since at least 1925 the U. S. Public Health Service has placed a limit of 0.10 ppm of lead in drinking water and a water supply may be rejected if the concentration is above this level.

The results of many analyses indicate that the mean daily lead intake of the average North American adult is about 0.3 mg of lead in food and beverages. This same amount is eliminated daily; hence there is an equilibrium between intake and elimination and there is no lead retention. An experiment in which an additional 0.3 mg of lead per day was added to the average normal intake of 0.3 mg, making a total of 0.6 mg per day, resulted in some lead retention. The safe level of lead ingestion in food and drink appears to lie between 0.3 mg and 0.6 mg per day. The limit of 0.1 ppm (0.1 mg per liter) of lead for drinking water therefore seems reasonable and satisfactory. The level apparently is not hard to meet as the results of the analysis of drinking water from 36 cities in the United States gave a mean value of 0.011 mg per liter with a range of 0.001 mg to 0.04 mg per liter.

Hygienic Standard for Lead in Paint

The American Standards Association has established "American Standard Specifications to Minimize Hazards to Children from Residual Surface Coating Materials." The standard was the result of action by a subcommittee of a Sectional Committee on Hazards to Children, Z66, organized on March 12, 1953. The scope of activity of the subcommittee was limited to the potential hazards to children such as might come from the handling and use of painted articles, the hazard being from toxicity of coatings chewed off and swallowed.

The standard specifications state that "a liquid coating material to be deemed suitable, from a health standpoint, for use on articles such as furniture, toys, etc., or for interior use in dwelling units where it might be chewed by children (a) shall not contain lead compounds of which the lead content (calculated as Pb) is in excess of 1% of the total weight of the contained solids (including pigments and drier). . . ." This standard is applicable to a specific use, and is the only standard of which the author is aware which limits the lead content of paint. It would appear logical and reasonable to assume that any standard dealing with the lead content of paint, from the viewpoint of a health hazard, would be based on scientific and technologic data and not on the unscientific concept that, simply because a substance is "toxic," its use should be arbitrarily limited. It should be a fundamental concept that a substance can be used if it is shown that its use for a particular purpose is safe, and that it cannot be excluded simply because it is classed as a poison.

Summary

It has been clearly demonstrated that lead occurs in the human body without any adverse effects, and that a toxic response depends on concentration. Satisfactory hygienic standards for lead have been established, and it has been demonstrated that lead can be used safely if the standards are used and used properly. The establishment of standards is not an objective per se, but rather a means of obtaining an objective — the prevention of harmful or objectionable effects. The figures given in the standards have meaning only when used by competent persons and interpreted within the framework of the comprehensive knowledge of the biological action of lead. Figures are not a substitute for sound judgment.

DISCUSSION

DR. MAY R. MAYERS: Unfortunately, standards are being used not exclusively by competent professional people, but by lay groups who, with the best intentions in the world, try to use them for special purposes. This presents some serious problems.

We meet employers, for example, who, in selecting the materials they wish to use, would like to be able to run down a list of safety standards and pick the one with the highest number, on the theory that it is safer to use than the others. They do not appreciate the fact that the way in which they will use the substance, its physical, chemical and biological properties — whether it is a primary irritant, a sensitizing agent or whatever — will make a tremendous difference in whether it can be used safely for a given purpose despite its relative position in the list of safety standards. In some substances there is a wide spread between a safe level and one which is highly dangerous. In others, the spread may be so small that exposure to toxic concentrations is difficult to avoid. And long-range effects are among the matters not easily incorporated in safety standards. It is important, therefore, to educate employers to understand that the materials they wish to use cannot be selected for safety on the basis of their respective position in a tabulation of accepted safety standards. Numbers always have something of an atmosphere of magic about them, which make them misleading.

Another lay group which tends to introduce confusion into the practical application of safety standards comprises those who wish to legislate them into code rules and regulations for purposes of enforcement. As Dr. Schrenk so well pointed out, safety standards provide excellent bench marks and guides for control of the industrial environment. But in routine enforcement of legal requirements, there are

many practical limitations to their usefulness. The number of air samples, for example, which can be taken in the ordinary course of law enforcement, is necessarily limited — sometimes to only one or two samples. This is apt to be inadequate to evaluate the extent and the nature of the exposure, particularly when surges or intermittent exposure are involved. Lay personnel do not fully appreciate the limitations of sampling techniques — particularly the need for this work to be done only by experienced professional people — and the limitations of laboratory procedures. They must be impressed with the fact that safety standards have meaning only in the hands of professional people who understand their limitations and how to interpret them.

Erroneous use of safety standards is also common in the adjudication of causal relation in claims for workmen's compensation. When a worker's exposure is shown to have been substantially within the limits of the safety standard, as evidenced by subsequent investigation of his exposure, this is apt to be construed as conclusive evidence that there is no causal relation between his illness and the exposure, regardless of the clinical picture or other medical evidence to the contrary. Two errors are involved in such cases. First, it is not always possible to obtain reliable data, after the event, as to precisely what his exposure was in terms of safety standards. Second, safety standards are useful primarily as guides for control of the industrial environment and the protection of the group. When safety standards are complied with in a workroom, the incidence of injury to health is minimized. But most differences between individuals continue to be important here as in every other branch of medicine. A diagnosis in an individual case is a medical conclusion on the basis of medical findings to which information of the occupational exposure makes an indispensable contribution. Safety standards cannot, however, be used per se to make the diagnosis, nor can they determine the question of causal relation.

I would say that the safety standard for lead poisoning has stood up remarkably well over the years. I believe this is due to the fact that there has been a tremendous experience with exposure to lead in humans. Standards based primarily upon animal experimentation tend to be weak because the results cannot be extrapolated to human exposure with any great degree of confidence. Our present lead standards are remarkably sound, in my opinion. There has been discussion here, and elsewhere, of developing separate standards for the different lead compounds based on differences in their physical, chemical and biological properties. Theoretically, it should be possible to make such distinctions with profit. However, one must bear in mind that every standard is in essence an approximation; and, since there are so many variables involved, I wonder whether it is wise to go into refinements of the basic standard. I wonder also whether lay groups would not be tempted to take such refinements too literally, and so come to regard the numbers in the standards as even more infallible than they now regard the over-all lead standard, thereby leading to even greater misuse.

DR. C. A. NAU: My question pertains to standards for drinking water. I am involved now with a patient who was referred to us and who has been under treatment from California to Texas for an illness that is still undiagnosed. She was referred to us by the hematologist. We found she was excreting considerable lead beyond the usual permissible limits.

In discussing with her the possible contact with lead that she might have, and in her bizarre medical history and experiences with doctors all over this country, I discovered one thing that intrigued me. That was that someone had suggested to her that she use alfalfa tea. I asked her to bring me some of her alfalfa tea, which she did. I found the alfalfa tea, the brewed tea, had a considerable quantity of lead in it, so then I asked her to bring me some of the tea in the package. She brought me the tea. I brewed the tea. It had no lead. I asked her how she made the tea. She said she was the first one to get up each morning. She went to the hot water faucet and drew water from the hot water faucet and made her tea and drank it. She has been doing that for a long time. This was the brew she brought me which contained about eight-tenths of a milligram of lead per liter of urine. In trying to find out whether there might be any relationship to the drinking water, I asked whether there were any lead pipes in the water line. She said no.

Their home had been built under FHA specifications. Finally, they dug up all of the water pipe and found 12 feet of lead pipe (¾ inch) between the city water main and their property, from the city main to their household supply line, and the first takeoff from the household supply line was to the hot water tank.

She was the first one up each morning, and drank from the hot water tank.

My question is: Is it still the common practice to use lead pipe from a main to a supply line, or are there still lead pipes in modern homes, and is this of any significance?

CHAIRMAN BOWDITCH: We are convened in the City of Chicago. Unless I am way off base, it is not merely permitted, but required by the City of Chicago that all services, meaning the pipe from the city main to the basement of the building, must be of lead.

MR. CARL WALTERS: It would seem to me, in the various times and occasions that some of us do have to defend ourselves in litigation cases, that accurate, established standards such as have been discussed here would be the one specific defense that we would have, in that it is an actual figure, and that it cannot be correlated, or rather, it cannot be used by a claimant's attorney.

In so many cases the claimant's attorney can nullify what the expert states by taking an entirely opposite view, by quoting some of the various doctors including Dr. Aub, Dr. Kehoe, Dr. Shilling, Dr. Schwartz and many others.

The attorney merely refers to and quotes, that part of a doctor's text that fits the claimant's complaints. He can, and often does, completely nullify what the expert states.

DR. MAY R. MAYERS: I certainly didn't want to give

the impression of undervaluing safety standards. I think they are immensely valuable, as Dr. Schrenk so well brought out. Since he covered that area so comprehensively, I have confined myself to pointing out some of the limitations when used by nonprofessional people, unaware of the dangers. I particularly wanted to stress the fact that numbers cannot be used as a substitute for medical diagnosis in workmen's compensation litigations.

MR. T. C. WATERS: Our state is blessed with medical schools and a very competent Commissioner of Health of the City of Baltimore who is present today, also a very competent State Director of Health. We have before us the consideration of the amendment to regulations relating to the permissible concentrations of materials.

I would like to underline what Dr. Schrenk has said in his concluding remarks, that these particular MAC values should be a guide to industry rather than be mandatory.

I cannot fail to reply to the remarks made a few moments ago expressing what to me is a pious hope about the establishment of these values. It may sound good in a courtroom, but when we come to defend cases and say that we have complied with these MAC values, that turns out to be not too real a defense. It still goes to the jury, and the jury, time after time, will find for the plaintiff.

Mediocrity on the March

The mental disease of the present generation is impatience of study, contempt of the great masters of ancient wisdom and a disposition to rely wholly upon unassisted genius and natural sagacity. The wits of these happy days have discovered a way to fame which the dull caution of our laborious ancestors never dared attempt; they cut the knots of sophistry which was formerly the business of years to untie, solve difficulties by sudden irradiations of intelligence and comprehend long processes of argument by immediate intuition.

This interesting paragraph was not written by an acute observer of some of the rank peculiarities of modern society but by Samuel Johnson over 200 years ago in his weekly magazine, *The Rambler*. It is particularly applicable to a segment of the population at the present time. Quotation marks were left off purposely for it leads us directly to some remarks.

Like every sensitive observer, Johnson was moved to savage indignation by what he saw, his emotions torn and frayed. Rather than try to change the social fabric, however, his remedy was to shock men back to sanity. For this he found satire and scorn more effective than enthusiastic preaching.

Those of us who are concerned about the shifty and slipshod methods of the workmen of today, the shady tactics of some citizens and the irresponsibility of a few politicians can understand that such nefarious practices are not new in the world. While these shilly-shally procedures are limited to a minority, nevertheless, they detract from the reputation of the large majority of citizens who try to do what is ethically and morally honorable.

The democratic process *per se* is valid whereby men are able to rise up and improve themselves but it does not always advance the best elements. Promotion should be on a basis of merit either before elevation to a higher position or from evidence of some improvement in ability after assuming new responsibilities. We have not been cognizant of much preparation for high office either before or after election in the majority of instances.

There has been a wave of antiintellectualism in recent years all over the world. Men of learning have been called "egg-heads" and their habitats described as ivory towers in a derogatory manner. Lesser men have been prone to detract from the abilities of those learned and capable individuals who applied themselves with zeal to academic education or practical training and advanced accordingly. Mediocre men have intimated that so-called egg-heads are straw men when in reality they deserve respect rather than derision because they are a little superior. The pursuit of excellence requires considerable road work and is not such a popular race as it should be.

Sometimes men band together for their mutual improvement and this is commendable. We would like to see the ethical and cultural values of America increased by evolution rather than by revolution. Mediocrity on the march seldom becomes very effective unless men of outstanding ability from other sources are employed for leadership and herein lies the possibility of exploitation.

Mediocrity is insurgent.

—Charles Sellers, M.D., in *Detroit Medical News*, November 24, 1958.

THE LEAD CONTENT OF WATER

from Red-Lead Painted Tanks

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For many years standpipes and tanks for water storage have been painted on the inside with red lead paints since, in the past, lead paints have been generally superior to paints containing other pigments.

The presence of lead in drinking water in sufficient amounts to cause intoxication has been noted occasionally. So far as I have been able to determine, the source of the lead usually has been lead pipe, and ordinarily in domestic plumbing. Previously I could have said it had invariably been lead pipe, but Dr. Kehoe pointed out that there have been other causes of lead in drinking water than lead piping. Even such pipe, as a rule, presents a serious problem only if the water is soft and acidic.

During the last war, the question was raised of the suitability of red lead paints in tanks used for potable water. Laboratory studies undertaken by the U. S. Public Health Service indicated that some lead was dissolved from panels coated with red lead paints. As a result of this finding, it was suggested that the use of lead paint in tanks and standpipes used for the storage of potable water be prohibited.

At the request of the Lead Industries Association, a study was made of the lead content of water from several standpipes which had been painted internally with lead paint. This study, which was begun in 1950, has involved analysis of 70 samples of water from 11 different standpipes coated with three different types of paint.

The paints involved were:

1. Red lead in linseed oil, referred to hereafter as Type I. This is the paint which in the past has been mainly used in water storage tanks.

2. Red lead in a phenolic vehicle, referred to as Type IV. This is currently the preferred paint in many quarters, being faster drying and supposedly more durable than Type I.

3. Lead chromate in a phenolic vehicle, referred to as E & F King paint. This paint has been widely used in New England.

Samples were taken from four standpipes immediately after painting. From three of these, samples were subsequently taken at intervals for virtually the entire life of the paint, five, eight and eight years respectively. The largest number of samples was taken from tanks painted with Type IV paint, as Table I shows, because our main interest, especially at the beginning of the study, was in Type IV paint.

TABLE I.

Paint	Number of Tanks	Number of Samples
Type I (oil base)	4	5
Type IV (phenolic base)	5	51
E & F King (lead chromate)	2	14
None (influent)		20

Three of the tanks coated with Type IV paint were in New Jersey. The remaining eight were in Massachusetts. They varied in size from 75,000 gallons to 3.7 million gallons. Samples were collected by engineers of the Massachusetts Department of Public Health, by waterworks personnel and by the writer. Most samples were drawn off from outlets adjacent to the standpipe, a few were dip samples, and some were from outlets somewhat removed from the tank.

Analysis

Since it was desirable to detect very small traces of lead, large samples (400 to 500 ml) were analyzed. The lead was concentrated by coprecipitation with calcium oxalate. This was found preferable to evaporation or direct extraction with dithizone. The determination was made with a dithizone colorimetric procedure. Analysis of knowns indicated complete recovery and an accuracy of ±10% if the lead content exceeded 0.02 mg/1.

Results

The results of the 90 analyses are summarized in Table II. By far the greatest number of samples contained a negligible amount of lead, less than .005 mg per liter. I have used the

terminology of milligram per liter. A small number contained between .006 mg and .010 mg per liter, an approximately equal number contained between .011 mg and .02 mg per liter. There were two samples that contained between .02 mg and .05 mg. One of these samples contained .05 mg per liter, which was taken from a tank painted about one year previous with the Type IV paint, but another sample taken at the same time had a negligible lead content. There were no samples in the range between .05 mg per liter and .1 mg per liter.

TABLE II.
SUMMARY OF RESULTS

Lead Content (mg/L)	Number of Samples	
	Standpipe	Influent
0.000 to 0.005	50	13
0.006 to 0.010	7	4
0.011 to 0.020	8	1
0.021 to 0.050	2	2
0.051 to 0.100	0	0
0.11 to 0.50	3	0

If you will recall Dr. Schrenk's paper, .1 mg per liter is the permissible limit for lead in drinking water. We found there were three samples that contained over .1 mg of lead per liter, and less than .5 mg. These samples are all from tanks not in active service, but used in stand-by service.

One of them was from a tank that had just been painted with E & F King paint. The other two were from a tank which had been painted about three years previously, with the Type I paint. Apparently the water in that tank had a very definite lead content.

TABLE III.
SUMMARY OF PANELS RESULTS

Coating	Lead Extracted (mg/day/sq. ft.) (average)	
	1st 2 weeks	1st 3 to 9 months
Type I and PbO	5.5	0.90
Type I	2.2	0.56
Type IV	0.31	0.10

How can we reconcile these results with the findings of Fairhall and Fraser of the Public Health Service that lead dissolves freely from lead paints such as those used in these standpipes?

The obvious explanation is that the water does not stay in the tank long enough to pick up appreciable amounts of lead. The three standpipes studied most thoroughly were in institutions where the daily water consumption approximated the tank capacity.

We have carried out a few panel studies in our laboratory and, in general, confirm the report of the Public Health Service, that appreciable amounts of lead are dissolved, especially from Type I paint. As a matter of fact, Type I paint with litharge added, which, we understand, is frequently used, gave off appreciably more lead during the first few months than the straight red lead in oil.

Our results, converted to mg of lead dissolved per square foot of surface per day, are summarized in Table III.

The first two weeks in which they were tested in water, the Type I paint with litharge gave off an average of 5.5 mg of lead per square foot per day. The straight Type I paint gave off less than half that amount, and the Type IV paint gave off one-twentieth as much. Now if we take the average extraction of lead for the first nine months, we find the rate is greatly reduced, and it amounts, on an average of the first nine months, including the first two weeks, to .9 mg per square foot per day for the Type I paint with litharge added, a little more than half that much for the Type I paint and about a tenth that much of the Type IV paint. Actually, with the Type IV paint, the experiment only ran a little over three months.

If we assume the same ratio of solution of lead from the interior of a given standpipe as was found in the panel experiment, we can compute the rate of water turnover needed to keep the lead content within specified limits. Such calculations for a standpipe 26 feet in diameter and 20 feet high are shown in Table IV. This is a small standpipe (about 100,000 gallons), and represents rather an unfavorable ratio of surface to volume.

TABLE IV.
TURNOVER OF WATER AND CALCULATED LEAD CONTENT

Paint	Time after Painting	Lead Content	Gallons of Water/day
Type I and PbO	1st 2 weeks	0.1 mg/l	31,000
	1st 9 months	0.01	51,000
Type I	1st 2 weeks	0.1	12,000
	1st 9 months	0.01	32,000
Type IV	1st 2 weeks	0.1	1,800
	1st 14 weeks	0.01	5,700

It is seen that even with oil base paints, a daily consumption of less than the capacity of the standpipe will result in a lead content, from the paint, of less than one-tenth the maximum allowable level. With the Type IV paint, a much lower consumption will yield the same results. With larger tanks, a lower turnover is needed to effect an equal dilution of the lead, since the area of the tank walls and bottom is less, in comparison with the volume, than in the smaller tanks. Conversely, with smaller standpipes a higher rate of water turnover would be needed for dilution of the lead.

I do not believe that any of those who object to the use of red lead paint in standpipes seri-

ously think that enough contamination of the drinking water will result to produce a significant number of cases of lead intoxication. The permissible limit of .1 mg per liter provides a substantial margin of safety for the average individual, as it should. And, according to our findings, this level was not even approached in most of the samples, nor would it be in most systems.

It has been proposed, however, that although harmful levels of lead are not produced in the drinking water, any increase at all in lead consumption is undesirable and should be prevented. I can go along with this argument to a certain extent. If all the water consumed by a large population contained lead right up to the permissible level, a careful statistical study might reveal marginal harmful effects to a small number of individuals with occupational or other exposures to lead, since the amount of additional lead intake required to produce intoxication would be somewhat reduced. As the lead content of the water is lowered substantially below .1 mg/1, however, the law of diminishing returns would apply. I doubt very much that any effect at all could be detected, by the most refined method, in a population whose water supply contained .01 mg/1 of lead, in comparison with one whose water was absolutely lead-free.

There are other much more important sources of lead intake than lead paint in water standpipes. One such source is domestic plumbing. By this I do not mean lead, but modern plumbing with iron, brass and bronze pipes and fittings. We recently analyzed samples of water in our office and in the home of one of my colleagues and myself, taking samples from the faucets and water coolers the first thing in the morning, and later after the water had run for some time. The results are given in Table V.

TABLE V.
LEAD IN WATER FROM PLUMBING

Source	Lead Content (mg/1) Morning Sample	Later Sample
Office	0.034	0.002
Home A	0.024	0.010
Home B	0.007	0.004

In each case the lead content of the water in the first sample was measurably greater than that of the second, and in two cases the difference was significant. These quantities of lead are insufficient to cause any concern, and anyone who advocated new plumbing in a house because of lead concentrations of this order would indeed be labeled an extremist. But, according to our findings, the lead hazard from paint in water tanks is even less.

Of course, our studies were limited to a relatively small number of tanks, all in the same section of the country. While some unfavorable conditions, notably the softness and acidity of the waters, which were mostly in the pH range 6. to 6.6, favored the extraction of lead, other factors, such as higher temperatures and chlorine content, may be more prevalent in other areas. It is my opinion, however, that the most important factor is the rate of turnover of water in the tank.

It could be within the realm of possibility, in isolated instances, that the water regularly consumed by a given population may have been stored in a standpipe for several days. Such situations, if they occur at all, would almost certainly involve relatively small numbers of people. In such cases it might be that some coating other than Type I paint would be advisable for the interior surface. It is exceedingly hard to visualize a water supply system, with a tank of comparable capacity to that of the tanks studied, where storage could be so prolonged that Type IV paint would be unsuitable, according to our results.

Conclusion

A study of the lead content of water from eleven standpipes painted with lead paint has been made. Of 70 samples of water, only three contained significant amounts of lead, and these were from tanks in stand-by service. Tests of the extraction of lead from panels coated with red lead oil paint indicate that no significant quantity of lead will be added to the average water supply by the paint if the average daily consumption approaches the capacity of the tank; and if a phenolic base paint with a red lead pigment is used, a substantially lower rate of turnover is essential to keep the lead concentration below significant levels.

All the evidence available indicates that only under extremely exceptional conditions, if at all, could the use of lead paint in standpipes for potable water be considered inadvisable from the standpoint of public health.

DISCUSSION

DR. HERBERT E. STOKINGER: I think we are probably in substantial agreement, although we arrived at the agreement by somewhat different lines of reasoning. I think there is no question that the amount of lead in our drinking water is of significant health concern to all of us.

Presently, the Public Health Service drinking water standards are being revised. This revision is in a downward direction from 0.1 parts per million to .05 parts per million. What is the reason behind this?

As you know, lead is a cumulative poison. It is

also an element to which there is no tolerance developed, as with, say, arsenic. The reason for this is not quite clear, but it apparently has to do with the rapid mobilization of the element from bone storage sites.

It has been shown by Dr. Kehoe and others that the amount of lead, that is, the tolerated dose daily is in the order of .5 mg per day. This is the tolerance dose.

Now this means that any amount above this value taken into the body and stored starts accumulating and results in effects on the health. Now where are the sources of this material? They are food, water, air and tobacco smoke. Quantitating these contributions from the various sources, Dr. Kehoe has shown in an extensive study that the food of the average person per day taken in is about .32 mg. It may run up as high, however, as 2. mg. This includes water which at the time he made these measurements contained .01 of a part per million throughout the country on the average. This has been quoted this morning.

Now the lead content of the air, (here is an interesting thing) for an approximate decade in which this has been measured, beginning say, with Clayton, Myers and Keenan's work in the Detroit-Windsor area, the level in air about 10 years ago was a few tenths of a part per million. At the present time, from results of our national air sampling network, this level has risen tenfold and seems to be still on the increase, so now we have an average of about three micrograms of lead per cubic meter of air, and it seems to be on the rise, owing to the increased auto traffic.

I should say that of the 20 cubic meters of air that is breathed a day, this contribution would amount to something in the order of .06 Pb. In tobacco smoke, lead contains the highest metal content of all the metals analyzed to date except sodium and potassium — higher than nickel, higher than arsenic, chromium, magnesium and other elements measured, and it amounts to about three-tenths of a microgram per puff. These are results that have been revealed recently by the Lorillard Company from Duke University, and in a heavy smoker this might amount to about .09 gm per day, assuming three packs per day smoked, and about 50% retention of the smoke.

You can see now without the use of an IBM calculator, if you add these materials up, there will be from the food and air and the smoke about .45 mg of lead, most of which will be retained.

Now this level, as you can see, is closely approaching the known tolerance limit. So the reasoning along those lines, is the basis for revising the Public Health Service standard for drinking water for lead down to .05 parts per million.

We might point out how easy this is to attain in waters that are not obtained from tanks that are painted with lead. The findings are from recent samples we made in a fifty mile area around Cincinnati in water that was stored in reservoirs and not in lead-painted tanks.

The values represent trivial contributions of lead in terms of about two-tenths to about two micrograms to five micrograms per liter, so we are well below the threshold limit of .05 parts per million suggested in natural waters that are not contaminated by lead paint.

What happens when we consider the amounts leached out of the different types of paint as determined by the work of Fairhall some years ago? The issue here, I think, is clear. The lead in the linseed oil base paint was dissolved in an exorbitant amount from the panels in comparison with other lead paints in which there was a minimal solubility, and with which we have no quarrel, i.e. the phenol and vinyl base paints.

In the first day there was 23 times the rate of solubility and the tenth day it was still dissolving nearly 11 times faster, so I think we are in no essential disagreement, and this is the fact: we would go along with the idea that it is all right to paint tanks with lead provided the linseed oil base paint is not used.

I realize this is practically a greater difficulty because of the fact that these other paints do not adhere so well, but that of course is a formulation and production problem which is not to be considered with health.

DR. KEHOE: I am obviously not in any point of difference with either Elkins or Stokinger, but I would like to add one comment concerning this quantity that Stokinger has spoken of as being the threshold quantity.

I wouldn't put the tolerable level, previously at 0.5 mg per day, as he has. I would simply say that, in balance experiments, we have observed that this level is somewhere between 1. mg per day and .5 mg per day. If someone wishes to go all the way down to the half, I wouldn't quarrel with him too much, but I would put it somewhat higher. Our estimate, therefore, of the safe level of daily intake of the normal individual is based on this fact, that above such a level of intake, some lead is retained regularly, giving rise to an accumulation within the body. This point, I repeat for emphasis, is somewhere between .5 mg and 1. mg per day. If one extrapolates beyond the period of experimental observations to predict what would happen in the course of a lifetime, and assumes that there is a straightline relationship (we have every reason to believe that it is, although we have not observed the facts for longer than five years), somewhere above this level of daily intake is a point at which one may accumulate in his body in a life time quantities of lead, which, in terms of industrial experience, may be dangerous.

Now there are several doubtful matters in this procedure, and perhaps this is one of those things to which a firm figure should not be given. I would merely say, we present evidence that it is somewhere between .5 and 1. mg of the anion lead (Pb^{++}) per day.

DR. J. H. FOULGER: As a poor toxicologist, I am getting a little confused by these standards. This morning we talked about the two-tenths of a cubic meter in the air in plants which we thought was safe. The average working man at perfect rest would have a respiratory exchange of about five

liters per minute. At work we will say four times that which amounts to about ten cubic meters per day. With .2 mg per cubic meter of inhaled air, he would have an intake of 2. mg of lead per day.

You have talked here of .1 mg per liter in water. The average man would drink about two liters of water a day. He would have an intake of .2 mg per liter per day. The Food and Drug Administration, in setting its tolerances over the years, has said the tolerance of a lead residue on an agricultural product shall not exceed 7. mg per kilogram of food; seven parts per million. According to their own data, the average man of 60 kilograms body weight (I don't think that is based on the United States; the average man is about 70 kilograms), but the average man of about 60 kilograms per body weight would take in about one and one-half kilograms of food per day which, at 7. mg per kilogram food, totals 10.5 mg of lead. My whole point in mentioning this is that we are talking about standards in Region A and Region B and Region C: The Food and Drug Administration and the state equivalent thereof; the State Compensation laws; the water standards of the U. S. Public Health Service. When are we going to get together and find out that the different standards we are using are incompatible? The best is probably the standard for the air, but the others, particularly the food, may be fallacious.

The Mass Mind and Ignorance

"A piece of Jade cannot become an object of art without shaping, and a man cannot come to know the moral law without education. Therefore the ancient kings regarded education as the first important factor in their efforts to establish order in a country."

—Advice to Fu Yueh by King Kaotsung of the Hsia Dynasty.

In an age of multiple crises stretching from Matsu to Little Rock, no single conflict can be isolated, either in time or space. The political and social philosophies of the shrinking contemporary world are seemingly so incompatible that there has been a tendency to view every issue as belonging to one opposite pole or the other.

In the face of such chaos and intemperance, the nation turns to the colleges and universities in search of leadership. Surely there, if anywhere, is the disinterested search for truth. Perhaps the young campus intellectuals may yet establish that temperate climate so needed by a world bent on extremes.

There is, however, a growing concern over the readiness of the American college student to assume these responsibilities. A recent survey by the Commission on the College Student from the American Council of Education states that the level of student ability has made the curriculum in some colleges obsolete, inappropriate, or devoid of challenge. Mass production in education has blunted the student's creativity.

Other evidence is cited in the Jacob Report, which, published in 1957 under the title *Changing Values in College*, emphasizes two deficiencies in the current college student. The first is the self-centeredness of the student and his lack of interest in outside affairs. The second is his trend towards conformity.

If the youth of today confuses the sterility of conformity with the necessity for cooperation; if he mistakes rugged individualism for selfish materialism, then he surely is echoing the confused values of his parents. Let us hope for him to achieve *both* intellectual independence and a sense of social responsibility which will lead him to more than an expedient and pragmatic role in life.

John Stuart Mill, as quoted in a current article by Arthur M. Schlesinger, Jr., states the problem thus: "The amount of eccentricity in a society has generally been proportional to the amount of genius, mental vigor and moral courage it contained. That so few now dare to be eccentric marks the chief danger of the time."

Mill's observation should give pause not only to the students and professors, but to parents and to citizens as well. Here is no plea for the fanatic, or for the Bohemian, but for him who dares to question, to think, and to care. Unless society, the school, and the home provide a milieu wherein such independence may thrive, we shall breed a generation of conformists quite as dangerous as their totalitarian opposites.

That which we fear most is the submission of the individual to the charlatan, to the demagogue, to the state. It is one thing to seek actively the Nirvana of conformity and another to submerge oneself in the mass mind through fear of being different.

The citizen of tomorrow must not be an isolated individual who leaves society to its fate, and neither must he be a mere worker, indistinguishable from all others in the colony. Man is a social animal, it is true, but a democracy presupposes the opportunity and the obligation for each genotype to make his maximum contribution to the society whose well-being is reciprocal to his own. If the young intellectual determines to seek only the opportune and the personally useful, the nation to which he belongs will not live long to count its useful days.

—Lufti M. Sa'di, M.D., in *Detroit Medical News*, December 15, 1958.

An Evaluation of
BLOOD LEAD ANALYSES

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The laboratory offers a number of tests and analyses which are useful in the diagnosis and control of lead poisoning. Each has its advantages and disadvantages. The stippled cell count, the basophilic aggregation test, and the urinary coproporphyrin determinations are simple and rapid, but they are not specific for lead poisoning because they indicate pathologic reaction in the body which may be due to other morbid states as well as to lead poisoning. Urinary and blood lead determinations possess the virtue of specificity for lead; however, the analytical procedures are time consuming and require considerable care and skill on the part of the analyst.

Urinary lead values show relatively large day to day variations although they correlate well with lead intake. Because of this correlation and the ease of obtaining samples, urinary lead values are widely used as a biologic test for the monitoring of lead exposures to indicate the need for further clinical and environmental controls. The analysis of urine for lead is somewhat, but not significantly, less difficult than the similar analysis of blood. In general, the concentration of lead in blood is considered to be more closely related to the clinical diagnosis of lead poisoning than are urinary lead values.[1,2,3,4,5,6] That other clinical signs and symptoms of lead intoxication may exist when there is no abnormal elevation of the blood lead and that such signs and symptoms may be absent when the blood lead concentrations are quite high, is a recognized enigma. Because of this, the ultimate diagnosis of lead poisoning depends on the skill of the physician in assessing the significance of the combination of laboratory results along with signs and symptoms in each case. Nonetheless, the determination of lead in blood remains one of the most valuable tests for lead poisoning. Often we have thought of lead poisoning only from an industrial standpoint where we know the individuals are exposed to lead. In such cases, some of the simpler screening tests have definite application because you have a known etiology. However, in other instances, particularly in lead poisoning in children or in adults who are not occupationally exposed to lead and for whom the source of the illness is not so apparent, the diagnosis of lead poisoning is more difficult and urinary and blood values become of extreme importance.

Over the course of years there have been numerous investigations to establish the normal limits of concentrations of lead in blood of individuals having no industrial or other special exposure to lead. In 1944, Cantarow and Trumper[5] in their book, *Lead Poisoning*, summarized the principal works on blood lead to that date. On the basis of these data concentrations above .08 mg lead per 100 milliliters of whole blood are believed to be abnormal and indicative of unusual absorption of lead. Values of 0.05 or less mg/100 ml were reported in 75% of normal subjects and 0.06 or less mg/100 ml in about 85%.

Since 1944 there have continued to be reports of studies to determine normal blood lead values.[7-22] Most of these have been in the foreign literature and may need to be carefully examined before applying the results to a consideration of a North American population. Quite interesting, however, is the fact that most of these reports give ranges and median values quite in agreement with previous and current work in this country. The significant deviations from this come principally from Japan[15,16] where an upper normal limit of 0.03 mg/100 gm is reported and from Italy[17,18] where the upper normal limit is given as 0.09 or 0.10 mg/100 gm. A few reports[19,20,21,22] from other European countries give either higher or lower values but most investigators report upper limits of 0.06 to 0.08 mg/100 gm, with the median values of about 0.04 mg/100 gm. Recent work favors the expression of milligrams or micrograms of lead

per 100 grams of whole blood rather than the expression per 100 milliliters as previously used. The lead values will be somewhat smaller numerically when expressed relative to the weight of blood rather than volume; however, the difference is so small as to have little significance relative to natural and analytical variations.

Blood lead concentrations in excess of 0.06 to 0.08 mg/100 gm are unquestionably indicative of a greater than normal absorption of lead. Values as high as 0.12 mg/100 gm are not uncommon among some industrial workers and others having an abnormal exposure to lead. The diagnostic significance of elevated levels of lead in blood and their correlation with clinical lead poisoning are not as well established as are the normal range of values.[5,6,12,21,23,24,25,26,27] While much of this uncertainty is due to physiopathologic factors in lead poisoning, a measure of it may be due to inconsistencies or errors in analyses of blood for lead. The latter may also account for some of the divergent reports on normal lead levels.

That the lead in the blood is concentrated for the most part in or on the red blood cells has been established and accepted for some years.[5,28,29] The proportion of lead in the serum increases with the total lead concentration in the blood. Some workers believe that increased lead in the serum after defibrination is associated with active manifestation of lead poisoning.

The actual chemical form in which lead is transported in the blood has not been definitely established. Various suggestions are colloidal dilead phosphate, lead diphosphoglycerate, a lead albuminate, or other phosphate or organic lead complexes.[5,28]

In the late fall of 1957, a reported increased potential for lead poisoning among children caused the U. S. Public Health Service to convene an ad hoc committee of experts to consider this problem. In the course of their deliberations, the importance of blood lead analyses in the diagnosis and control of lead poisoning was repeatedly emphasized. The ensuing discussion of the difficulties and exacting requirements of reliable microanalysis for lead in blood developed the opinion that the availability and adequacy of such analyses were questionable in many areas and that in reality there are only a few laboratories doing precise and reliable blood lead determinations. The need for some definitive evaluation of this situation was apparent. Accordingly, in the spring of 1958, the Occupational Health Program, U. S. Public Health Service, agreed to coordinate a project for the voluntary cooperative evaluation of analyses for lead in blood.

A plan was drawn up for the submission to cooperating laboratories of several sets of blood samples with known amounts of added lead to be prepared by the Occupational Health Program laboratories for analysis. The principal objectives of the project were stated: (a) To secure a statistical appraisal of the general competence in this analytical diagnostic service, and (b) To provide participating laboratories with a controlled self-appraisal of their techniques of blood lead determinations.

This plan was presented to the Conference of State and Territorial Health Laboratory Directors and to the American Conference of Governmental Industrial Hygienists and received the endorsement of both of these groups.

Subsequently the health officer of each state was requested to designate and to secure the participation of some clinical and industrial hygiene laboratories having responsibility for blood lead analyses in his state. The inclusion of every possible laboratory was neither anticipated nor intended as the project was conceived to evaluate the general level of analytic performance. It follows, of course, that should the study reveal serious inadequacies, further action should be taken by those laboratories to improve their methods and techniques. A roster of 50 participating laboratories was obtained and the first set of samples has been prepared and mailed in duplicate to them.

Sixteen pints of recently outdated, citrated blood were obtained from a blood bank and combined into a single reservoir pool. This pool was mixed thoroughly; then, with continued agitation, was divided into six equal portions. To each of five of these portions, a known amount of lead was added. After mixing, 10 milliliter aliquots of these samples were measured into lead-free test tubes and stoppered. All samples were kept under refrigeration insofar as practical during preparation and until shipment. Extreme care was taken to avoid contamination and to assure uniform mixing at all times.

The lead was added as a standard solution of lead chloride which was measured into the portions of blood with a microburette. The lead chloride had been highly purified by multiple recrystallizations. An accurately weighed portion of lead chloride was dissolved in double-distilled water with a small amount of redistilled hydrochloric acid added. The concentration of lead in the standard was determined by calculation and by analysis. A further check of this standard was made against spectrographically pure lead nitrate obtained from a spectrographic supply laboratory.

The chloride of lead was used in preparing these samples because of the high purity of the material available, and the compatibility with other chlorides already in the blood. Others have

used the nitrate or the acetate but there is no indication of any special virtue of these anions. Tests of our sample with the highest concentration showed that the lead was somewhat more than half in the cells and the remainder in the serum, which indicated that it was going somewhat in the form that we might expect to occur naturally.

Replicate specimens of each sample were analyzed in our laboratory immediately after preparation of the samples and on four other occasions spaced over the period of a month. We used the procedure often referred to as the "U.S.P.H.S. Method";[30] after wet ashing with nitric acid, the lead is determined by a mixed color dithizone procedure. The mean value of 10 analyses of the pooled blood without any lead added was taken as the blank or base line concentration of lead. The concentrations of the five samples with added lead were calculated by adding to this base line the known values of the standard lead chloride solution added to each. Table I shows these calculated concentrations as compared with maximum and minimum individual values and the mean of all values of analyses of the several samples.

TABLE I.

	Results of Analyses, mg/100 gm.		
Calculated Conc. mg/100 gm.	Maximum	Minimum	Mean
(0.026)	0.029	0.024	0.026
0.055	0.055	0.045	0.050
0.084	0.082	0.075	0.078
0.142	0.136	0.120	0.129
0.258	0.258	0.214	0.242
0.315	0.307	0.275	0.297

The methods of analyses to be used by the participating laboratories were not specified. Each laboratory was asked to determine the lead in the samples by whatever procedure they would normally use. The object of the project is to learn how well blood lead analyses are being done; not to compare methods at this time. We realize that there are a variety of procedures which will give acceptable analyses when properly used. The American Public Health Association publication, *Methods for Determining Lead in Air and in Biological Materials*,[30] discusses a number of procedures in detail and gives an extensive bibliography on the several basic techniques, including the "U.S.P.H.S Method."

At this time, most of the participating laboratories have not reported the results of their analyses, and we can offer only a few comments on the basis of limited data. Significant deviations from the calculated values occur mostly on the low side, and more often in the samples of high lead concentration. We are inclined to believe that such losses of lead are occurring during the ashing of the samples. This is based on our own experience.

Some error may be due to the absorption of lead in stoppers that were used. This point is under investigation at the moment, and I cannot tell you whether that is the trouble or not. If it is not that, it must be faulty analysis.

Contamination of a sample during analysis in the laboratory appears to be quite rare. Those samples would offer no indication of the degree or frequency of contamination which might occur in the collection of actual specimens from patients.

Although we do not have the final results, we feel that this project to evaluate the analyses of lead in blood will prove to be very worthwhile and will have a beneficial effect on the accuracy and reliability of blood lead analyses in general. Such an evaluation is a project which any laboratory or group of laboratories may carry out for their own benefit and information. Indeed, every laboratory doing determinations of blood lead values should appraise its techniques in this manner at reasonably frequent intervals. Such appraisal should certainly include the entire procedure on actual blood samples and not be content with analyses of aqueous solutions of known lead concentrations. The importance and the difficulties of blood lead determinations require such vigilance to prevent backsliding into unreliable or erroneous work.

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DISCUSSION

MR. W. C. L. HEMEON: I am curious to know what you mean by "disturbing." Aren't you going to tell us what the spread in the analyses was in the various laboratories?

MR. BYERS: At this moment I can't tell you. We have not analyzed the data. I have looked over what reports have come in, and at the time less than half of the results were in.

By disturbing, though, I mean that there were an observable number of reports which were sufficiently low that values of 250 to 300 micrograms of lead would have been reported as practically normal —say 100 micrograms. Values as much as 70% low.

I wanted to mention that this matter of the stoppers has to be worked out. Everybody has worried about contamination of the sample from the stoppers, but here we find a problem which indicates either poor analysis or absorption of the lead by the stoppers.

MR. W. M. PALLIES: None of our blood samples are citrated. Do you think that this is relevant? Our samples usually are clotted. The cells are not free to move, so only those at the top of the tube come in contact with the stopper where adsorption can take place.

MR. BYERS: We have assumed it was not due to the citration of the blood in view of the fact that we can get an analysis with better than 90% recovery after having blood on hand for as much as three months.

The only time that we had results which were excessively low was when we mailed ourselves some samples. The loss happened in going through the mail.

DR. R. A. KEHOE: Mr. Byers has said there are situations in which individuals with lead intoxication have lower concentrations in the blood than those that we generally regard as significant. This I do not believe. It is possible for the individual who has lead intoxication and whose blood has not been analyzed until sometime after the onset of his illness to have a relatively low concentration of lead, i.e., below 80 micrograms per 100 grams of whole blood. That is to say that the illness has begun and still persists. Meanwhile the blood values are dropping, and they may be well below 80 micrograms by the time one sees the patient. This is not the point. What were the results at the time the patient became ill? I can say that, over a period now of 15 years during which we have carried out thousands of analyses per year, and have investigated some thousands of suspected or actual cases of lead intoxication, we have never seen intoxication in any adult or child who had less than 80 micrograms of lead in his blood by the methods of analysis which we use, and I do not believe it is possible to have lead intoxication in association with blood levels anywhere within the alleged normal range up to .06, nor do I believe that intoxication occurs except at levels above, and in many instances well above, 80 micrograms of lead per 100 grams of whole blood.

Don't mistake my words as meaning that values above 80 micrograms demonstrate that lead poisoning exists. This is not true. I am only saying there is a point of lead concentration in the body and in the blood below which intoxication never occurs, and to this there is no exception, in our experience.

This is important because it brings the question of susceptibility into issue. Is our standard for measuring danger subject to the vagaries of susceptibility? The answer is that we have no evidence, no reason for believing that there is any kind of susceptibility to lead which results in intoxication, if the level of lead concentration in the blood is lower than a certain threshold level. This level is very near and somewhat below 80 micrograms per 100 grams.

DR. FOULGER: Mr. Byers has used the technique of adding an external inorganic compound to an organic complex which actually is a very important one. I know it is popular, but the fact is that the addition to a fluid outside the body of any chemical does not reproduce the conditions which surround the chemical after metabolism in the body, and excretion from the kidney with body fluid. The lead compound, whatever it may be, added to urine is not of necessity in the same chemical or physical condition, and particularly chemical, that a lead compound excreted in urine would be. That is due to the very complex chemistry of proteins and lipoproteins in the body.

It so happens in the chemical analysis for lead, one ashes the dry urine and therefore destroys any chemical complexes which may be specific to metabolism, but this procedure would not apply to mercury, for example, or selenium, or tellurium or any other metal. The discrepancies between the samples, Mr. Byers has suggested, are due to the stoppers. Rubber stoppers, unless they are made of latex rubber without any antioxidants whatever, contain sulphur compounds. He may have the right solution to his low values. On the other hand, even

if he should obtain latex stoppers, they might also produce lead or lead complexes.

I would suggest that he test with stoppers made of a synthetic material say, Teflon or Keef, or something of that type which we know does not absorb chemicals.

MR. K. W. NELSON: I quote Mr. Byers: "Urinary lead values show relatively large day to day variations although they correlate well with lead intake." Certainly that is true. Certainly it is true also that correction of urinary lead values to a mean urine specific gravity of 1.024, according to the method of Levine and Fahey, does very much to iron out these fluctuations. Any laboratory analyzing urine specimens should correct its findings for urine specific gravity: specific gravities taken with a calibrated urinometer and specific gravities corrected to a standard temperature.

Mr. Byers said, "In general the concentration of lead in blood is considered to be more closely related to the clinical diagnosis of lead poisoning than are urinary lead values."

I note that in his references he has omitted the paper by Dr. Pinto and others which was concerned with the correlation of various tests with clinical lead poisoning. The paper concluded that urinary lead and blood lead values more closely correlated with clinical lead intoxication than any other laboratory tests. If either had the edge, it was the urinary lead values.

Mr. Byers said, "The lead in the blood is concentrated for the most part in or on the red blood cells and that fact has been established and accepted for some years." In April of this year a paper by Teisinger, et al, in the *Archives of Industrial Health* reported the results of investigating the elution of lead from erythrocytes by solutions of EDTA in varying concentrations. The paper studied the effects of concentration and time, the rates of reaction, etc., and produced some very interesting data.

My own belief is that urinary lead and blood lead values should correlate very closely. The reason they have not is perhaps that the blood lead values have been erroneous. The disagreement among laboratories, as reported by Mr. Byers, would so indicate.

Certainly if lead is in the blood in association with red blood cells, it passes to the urine by passing through the plasma, through the kidney and into the urine. There must be, then, an equilibrium between lead in the red blood cells, lead in the serum and lead in the urine. Until we know the physio-chemical characteristics of these equilibria, we shall not be able to use the data we have with any degree of certainty. In other words, we can't be sure of the exact quantitative relationships.

It seems to me that in this particular area we have a need for a great deal of research. Whether industry can do it or whether government can do it, I don't know, but I hope someone does it in the very near future.

Diatomite Dust

The processing of diatomite, a versatile nonmetallic mineral composed of siliceous skeletons of microscopic, unicellular, aquatic plants, assumed significant proportions during World War II. Concurrent with the growth of the industry, increasing interest was focused on the potential lung disease problem associated with exposure of workers to diatomite dust in its various forms. By the later 1940's, sufficient evidence became available relating the development of a disabling pneumoconiosis to certain exposures in this industry.

U. S. Public Health Service study findings confirm the hypothesis that exposure to cristobalite-containing diatomite, which is produced in calcining the natural product, is the major pulmonary hazard in the diatomite industry and that amorphous or natural diatomite is distinctly less hazardous. Adequate data are not yet available upon which to establish firm maximum allowable concentrations covering the different forms of diatomite. Present information, however, indicates that atmospheric exposure to diatomite containing over 5% cristobalite should not exceed five million particles per cubic foot of air. Similarly, atmospheric exposures to amorphous diatomite should be kept under 20 million particles per cubic foot of air until data are available to define its biologic activity, including its effect upon superimposed infections.

As a result of this study, the diatomite pneumoconiosis problem has been more precisely defined, enabling industry to strengthen its control program. Recommendations emphasize engineering measures to reduce diatomite exposures, the display of suitable caution labels on shipping containers where indicated, the periodic medical examination of workers and frequent epidemiologic assessment of the pulmonary status of the employees.

Copies of the report, entitled "Pneumoconiosis in Diatomite Mining and Processing" (Public Health Service Publication No. 601) are available from the Public Health Service, U. S. Department of Health, Education, and Welfare, Washington 25, D. C.

PRECAUTIONARY LABELING OF LEAD PRODUCTS

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The common law of the United States and of England places upon anyone who manufactures, sells, loans or gives away an article which is potentially harmful the duty of warning the user of any hazards involved in the use. The duty may extend also to those in the immediate vicinity of use.

The American Law Institute prestatement of the Law of Torts extends this and says that if, because of youth or inexperience or for any other reason, the user cannot take full cognizance of the warning, the duty is still stronger.

There are three key words in this — harmful, hazard, warning. I think anyone who has had any experience with toxicology will agree that individual chemical compounds, all of them, may be harmful under certain conditions of use. But the complexes of these compounds, colloidal complexes or such complexes as chelates (such as lead with EDTA) are not of necessity harmful. Hazard may be considered as the probability that a vulnerable individual will meet a harmful situation. Hazard involves many factors. Those of the medicolegal point of view might differ from those of the legal point of view.

I am sure that Mr. Waters and Mr. Johnson will describe what the courts have ruled as to the legal meaning of hazard, but hazard includes not merely the intrinsic toxicology of a compound. It includes also the route by which that compound may enter the body.

There may be a question as to whether that route is a route of entry under the conditions of use, and further the question as to whether the susceptible individual is in such a condition physiologically and perhaps clinically, that that route or that potential of entry may afford a possibility of harm to him.

Warnings may be given in two ways, by precautionary labeling directly on the container, precautionary labels, they are termed legally, or by labeling which includes any additional information either on the container or in the form of pamphlets accompanying the container at sale or sent through the mail in any way associated with that sale.

It might also include the statements of salesmen. We recently had a very difficult situation in Missouri, in which the plaintiff claimed that while we had sent out a warning letter not to use a certain compound to produce a certain product, a salesman had said, "Ignore the letter."

It is ridiculous if the warning on the labels should not jibe with the labeling. It is perfectly silly to write a label which says that it is safe, and then in your communication to the users in any form say, "but under these conditions you must use this or that precaution." I assure you with certainty that common pleas courts will look upon this practice with suspicion and so will the Federal Trade Commission. Having been a member since its inception, or at least a consultant to, and a member of, the Labeling and Precautionary Information Committee of the Manufacturing Chemists' Association, I have had the opportunity over some 14 years to read and discuss practically all the legislation on labeling that has been introduced into state or federal legislatures in this country. Not merely because I am a member of the Committee, but because I have a wide knowledge of this labeling problem, I am certainly in favor of the basic principles of labeling which the Manufacturing Chemists' Association's committee has established.

These principles require that a precautionary label should contain the following information: first, the name of the compound; preferably the true chemical name. It should not be hidden in a trick name. Sometimes, of course, in the case of modern insecticides or even medicinal needs, the long chemical name would take about ten miles of type. In this case someone has invented a popular name, but still the chemical name should be there.

Second, there should be a word indicating the relative instensity of the hazard: "danger" for very hazardous compounds; "warning" for less hazardous; "caution" for least hazardous. When a compound is highly hazardous, it is suggested that there be added the term "poison" with the skull and crossbones and antidote. Because this is a very limited group of compounds, the term "poison" is not considered a definition, but a word applied to a specific group, which group is set up by specific toxicological tests or by human experience.

In this labeling program, of course, we find that some states have already said that such-and-such a compound should be called poison. In that case no labeling system can override the law of a state or the federal government, but there has been some misunderstanding of the use of the word "poison." It is merely a term used for a limited number of highly hazardous compounds in addition to all other warnings.

After having laid down the degree of hazard one adds a statement as to the route of hazard; by inhalation, by skin absorption, by swallowing; although in industrial products that is seldom the case. One follows up by a brief description of simple methods of avoiding the hazard. "Do not inhale vapor." "Do not inhale spray mist." "Avoid contact with the skin or eyes," and further still, simple remedial methods in case of contact with the eyes. "Flush thoroughly for at least 15 minutes with copious quantities of fresh water," or in the case of the skin "flush thoroughly with plenty of water."

That is the principle of labeling which I think, if accepted, can be applied to any field of labeling regardless of arguments to the contrary.

Now how does this apply to lead? First of all, the ordinary lead compounds as they may be presented to a factory for fabrication into other compounds can, like all initial chemical compounds, be considered as potentially harmful. The extent to which they are harmful depends upon their physical properties as well as the toxicology. If lead gets into the body in any form, it is harmful if it arrives in the body in the bloodstream and next to the tissues in adequate concentration.

Lead compounds may be dusty. Therefore, the initial package of lead compounds if it should contain a dusty compound should be labeled against the hazard from inhalation of dust.

Some lead compounds may be in solution. Some are intended for use by spraying. If they are simple lead compounds (such as lead arsenate in the insecticide field), they are not chelates. They are not colloidal complexes. There should be a warning as to the hazard from sprays.

I doubt whether one can differentiate in this field of labeling between the solubilities of different simple lead compounds. It is quite true that in the test tube lead chromate or lead chloride or lead sulphate might be less soluble than lead acetate, but I can't forget that to chemists, one of the most insoluble compounds of all is silica. Yet we have silicosis.

The solubility in the test tube in water or any other ordinary solvent that we use in the test tube is not of necessity comparable to the solubility in the tissues of the human body. I think we are "straining at a gnat and swallowing a camel" if we try in the labeling field to differentiate between the solubility of lead oxide and lead chromate.

Mind you, this question of hazards is not a question of concentration. It is a question of whether there could be harm.

We have heard discussion this morning of the one field in which an absolute standard seems to have been set. In New York City there is an ordinance requiring that a compound containing more than 1% lead paint should be so labeled. There is the American Standards Association standard which says that such paint products should not be advocated for use on interiors or on toys or in places which may be accessible to chewing by young children. That is a sort of absolute standard.

There has been a lot of dispute as to how it was founded. Now I was on the Z66 Subcommittee of the A.S.A. which established it, and I was one of the group, including Dr. Lanza and Dr. Cranch, who finally set up this 1% level. It was based on these considerations which in turn came from information we obtained from the paint industry. It was considered that the average paint containing lead contains about 60% by weight of solids. It is considered further that one gallon of an average paint, painted as one coat on a surface, will cover about 500 square feet, and by using the equivalent dimensions of feet and gallons and centimeters and milligrams, we concluded that a child would take in one milligram of lead if it ate about one and a half to two square inches of paint.

It was considered also that surely the parent would notice that amount of chewing. In a later report, which I was given confidentially, Dr. Kehoe has come to the conclusion that a child of three years of age must ingest about seven grams of a paint in order to get lead poisoning, and if it should be a paint containing 5% lead, it should be about six times that weight. That will mean 42 gm of paint for the child, but our A.S.A. Standard would require that the child eat about 210 grams of that paint, that is, seven ounces, if he were three years of age, to get lead poisoning.

I think that is a safe standard. How did that standard come about? It came about, of course, because of the concern over children having chewed chips of old paint that had flaked off the walls of old tenement buildings, painted years ago at a time when there was no differentiation between exterior and interior paints and lead could reach very high concentration in the paints on the market.

It does not necessarily apply to present considerations. The agitation for that specific form of standard came from a medical group who are now agitating for federal laws in the labeling field.

I am a physician. I think it a very serious situation that of our 82 medical schools of various degrees (that is, various durations of education) according to last year's A.M.A. report, only six have courses on toxicology. The development of absolute standards established by statute does not only come from lay people as Dr. Mayers and Dr. Schrenk said, but it comes from people who really do not know what they are talking about.

The trouble is that if we do set those standards, we are almost guaranteeing that they apply under all conditions. They do not necessarily apply under all conditions.

To come back to the labeling of lead compounds, the example of New York State shows that some of the situations entering common law are now entering into statutory law, usually criminal laws. There is a great tendency for people in the chemical and other industries to think that if they have conformed to statutory law in their vicinity, they are protected. That is wrong.

I might conform to a federal law on the labeling of an insecticide, or the labeling of a food. I am not protected before a jury or a court in a common pleas court in a suit for negligence by mere apparent compliance with the simplest letter of the law.

I must use good faith. I must acquire all the information I can about my own product, and I must in good faith transmit that information to anyone to whom I sell or loan or give my product.

DISCUSSION

DR. LOUIS W. SPOLYAR: Since there is no uniformity of either a legal or scientific opinion as to what constitutes a poison, I am impressed by a statement made by the 1956 American Medical Association Committee on Toxicology in that it tends to permit a broader concept as to what is, or is not, a poison. Their statement is as follows: "Since a precise definition that would fit all circumstances is not possible, the committee felt that any substance that, when improperly used, may produce harm by chemical action should be provided with an appropriate precautionary label statement. Such precautionary statements should provide warnings for different categories of hazards."

My particular fondness for this statement lies in the fact that it accepts a dual concept of what a poison is. It permits one to accept two physiological behaviors of a poison. First, the acute, violent upset of our normal physiological processes; and second, the more subtle but perceptible chronic physiological change. Thus, emphasis need not always be placed on accidental single exposures with the material.

This flexibility of definition is essential in considering the application of precautionary labels for it provides for the logical use of precautionary labels to materials that may produce long-term adverse effects — as exemplified in the occasional improper use of a household product.

Since we are discussing lead and lead compounds primarily, it is apparent that the acute accidental exposure, with a few exceptions, is not the major problem. In general, lead "improperly used" tends to create an exposure producing drawn out body changes in our general physiology. It would appear, then, that household, as well as industrial products, containing lead should have a precautionary label. Further, I would like to reemphasize Dr. Foulger's statement suggesting labeling should not depreciate the significance of that hazard. Through such intellectual honesty labels become meaningful.

Dr. Foulger indicated that labeling in compliance with a law does not necessarily solve the problem. To illustrate this, I would like to review some statistics relative to the operation of the poison control center in Indianapolis. Incidentally, I am not associated with this center. Dr. Nester, Director of the Indianapolis City Health Department, was kind enough to let me have these data.

These statistics reveal areas that at least are food for thought. For example, there were 289 cases of children treated at the poison center. Of those 289 cases, 208 were due to ingestion of medicinals. Of this 208, 130 children swallowed aspirin and 10 ate Ex-Lax, the remainder being prescription items. With the exception of aspirin and the Ex-Lax, the prescription items carried no warning labels of any kind.

Of the 81 children exposed to so-called household products, 35 were exposed to pesticides, 19 to cleaning and polishing materials, seven to petroleum distillates, six to turpentine, and five to paint.

The pesticides had labels on them. The greatest number were exposed to medication, and as a physician, I wonder if we aren't at the stage where we should write more on a prescription than just the "Take two or three times a day," but also as part of the directions a warning label such as "Keep away from children."

In general, the greatest activity of most poison control centers lies in the area of treatment for ingestion of medicines — primarily prescription items.

We have a household product labeling law in

Indiana, but under the circumstances cited, the labeling law was helpful in but a few instances.

The application of such labels to household products becomes a task due to space restrictions of small packages. Since lead bearing paints constitute one of the chief sources of lead poisoning in children, may I suggest, for this product at least, that the precautionary label advising that this product is not to be used for interior finishing of walls, be placed on the lid of the can and not as part of the product, name and "directions for use" label. If it is on the lid of the can, the "do it yourselfer" would more readily see the label as he pries the lid open. Further, this space, normally not used but always seen, would make it possible to use larger printed type and thus may facilitate recognition that the material is not to be used indoors. This may reduce the problem of lead absorption in children, which as you know is primarily due to eating flakes of old lead bearing paints formerly used as interior finishes.

DR. FOULGER: While lead compounds have been singled out in some communities on the basis of sentiment rather than fact, for special labeling, the labeling problem is the same for all compounds. It is equally serious or not serious according to the hazard which your compounds afford.

It is the duty of everybody who makes or sells or gives away a compound to know what it will do. The fact that for over 10 or 12 years an increasing proportion of home injuries — I won't say poisoning because many of them are not — home exposures to, or home ingestion of, chemical compounds has been from drugs rather than from industrial materials, of course, weakens the case for some groups such as the AMA Committee on Toxicology.

Don't forget that under the common law the responsibility is yours, and under the common law you may pay six hundred thousand dollars in damages, not just the two or three thousand dollars you pay under the statutory regulations.

CHAIRMAN McGEE: My first contact with what proved to be actual clinical lead intoxication occurred in 1932. There was admitted to the ward service of the City-County Hospital in Dallas, Texas, a man with colic. By some mischance he did not receive surgery that evening for appendicitis and the next morning the medical service was invited to work out on him as a teaching subject in diagnosis for the house officers and senior students who were clinical clerks. That was my assignment since I was on the service at that time.

As a result of our findings from the history and examination, my curiosity led me to make my first visit to a plant in the role of a physician. This was a small plant operation during the depression. In the typical American spirit, a young entrepreneur of limited financing was attempting salvage operations to recover lead from scrap. He had hired a number of Negro laborers. Our patient was one of them.

The business owner said, "Doctor, five or six of our boys have had similar trouble. I wonder if there might not be a problem here. I have asked a lot of people, but nobody seemed to be interested in it."

As a result of his cooperation, lots of spare time in 1932 for a young internist in Dallas, and the help of Professor Hambleton of the Physiology Department in the medical school, we obtained a corner of the laboratory and, with Aub's publications as our bible, proceeded to do urinary lead analyses. We demonstrated lead intoxication in three of the workers and increased lead absorption, with no signs of intoxication in a few of the other workers. The result was that we were able to help the entrepreneur with his salvage operation and I hope he is still in business.

I learned two things from that experience. Number one was the fact that the typical businessman has an open mind and welcomes anyone who sincerely wants to help him. Secondly, the most grateful patients that I have ever had have been those in an industrial operation when a physician can do one of two things; help them with a genuine problem or reassure them with the problem they have imagined or feared.

MR. ARTHUR JOHNSON: With respect to labeling, a point that everybody knows perfectly well, but it has not been expressed at this meeting and it might just as well be tucked into the record, much has been made of the fact that you can understand and believe the law and comply with the law — that is what Dr. Foulger said — but you have to demonstrate good faith, all of which we understand and agree to.

The fact remains that none, or all of those three things accomplished, will let you off. The best that labeling does for you is to provide some evidence that is admissible in the trial of your case, and the jury will decide how much weight they want to give it.

Just a point that it is not prima facie evidence, that you have absolved yourself from all liability, you merely have some defense that you can present as evidence, and the judge has to put it before the jury as good evidence.

In our clinical experience, that picture shown by Dr. Williams represents an extreme example. It is not reprentative of the usual situation.

I have two additional comments on the labeling of paint. Childhood plumbism is found almost exclusively in slum areas where lead-containing paints have fallen into a deteriorated state. Poisoning rarely occurs where surfaces are maintained in a good state of repair. Labeling of paints will help "do-it-yourself" parents and home owners in selecting safe paints for indoor surfaces and children's toys and furniture. Labeling will not solve the problem of deterioration. If communities wish to reduce their incidence of childhood plumbism they must acknowledge and implement the need for maintaining houses in a good state of repair.

Common Errors in the DIAGNOSIS OF PLUMBISM

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Today few diseases are as easy to diagnose as industrially induced plumbism. The area of contact is not elusive, the symptoms of 99% of all cases are well defined and the laboratory results, when procured by efficient techniques, are generally conclusive. Little of this can be said of most occupational diseases.

As a preface to any remarks on the diagnosis of plumbism it appears logical to accept this viewpoint, that whatever be the present attitude towards the value of diagnosis in general medicine, it will be reflected in occupational medicine. That there has been a deterioration in the art of diagnosis is obvious; due, no doubt, to the profession's overwhelming interest in the spectacular. Down the hallway of medicine as we pass hatracks we indifferently toss a diagnostic hat without looking to see if it landed on the right peg. We hurry on to a room on the door of which is emblazoned in gold letters T-H-E-R-A-P-Y. Therein is to be found the drama of medicine, likely as not being televised to a palpitating public. Also therein we find the means to cure our patient before a diagnosis is correctly established.

Nor should any concern over the decadence of diagnosis ignore the supplanting of our senses by the employment of numerous gadgets, contraptions and multiple laboratory procedures. To illustrate this employment of the extreme need I cite anything other than the seeming miles of paper which fall to the floor in a heap as the action of the heart is being recorded. The point is that while there may be a handful of specialists able to interpret 20 or more electrocardiographic leads, most all other physicians are confused.

Obviously there are many more factors which divert accuracy of diagnosis. Sufficient is the intimation that if the physician ignores, or is disinterested in, the basic principles of diagnosis in general medicine, he is likely to approach the occupational disease diagnosis dissolutely. It is not contended here that all of the common errors in the diagnosis of plumbism stem from the attitude or pitfalls just reviewed. There are additional factors which demand our attention.

Occupational History

It is in this area that erroneous conclusions are initiated. It does not fall within the purpose of this paper to outline the proper method of obtaining an adequate occupational history. I do wish to point out that in obtaining such a history we physicians are woefully inept at obtaining *all* of the facts. To again refer to general medicine, the patient suffering from acute appendicitis, gall stones or a coronary attack, presents signs and symptoms of well defined and recognizable clinical entities. But with most occupational diseases this is not so. Almost always there is a considerable degree of mystery. There has been an assault by an insidious criminal. To obtain conclusive evidence convicting the guilty agent requires adherence to a process of inquiry similar to that employed by the detective or newspaper reporter who seeks to obtain the complete story. How? When? Where? Why? are questions which must be pinpointed and then repeated and repeated. The question and answer period spent within the consultation room is invariably of much more value in plumbism than is the physical examination. If the physician is still not satisfied that he has gained the whole story he must further his detection by a plant investigation.

The Occupational Environment

The number of small plants in America engaged in manufacturing storage batteries or pottery or reclaiming lead from scrap metal is unknown. It is known that when the occasion demands, the majority of such plants usually use the service of the physician practicing in the vicinity. Of these physicians only the exceptional one ever surveys the plant he serves. Another group concerned in this problem is the specialist (usually the internist) to whom is referred the

alleged or actual case of plumbism involved in medicolegal controversy. From this group are derived opinions which again are rarely based upon knowledge of the occupational environment. Invariably the members of these two groups have never seen grid casting or pasting or burning or stacking. They have no first hand knowledge of the absence, presence or efficiency of control measures. Lacking all this information they cannot comprehend the jargon of the worker whom they see in their office. How then can they get the story of how, when, where and why? This situation is certainly one from which diagnostic errors commonly arise.

Errors Residing in Laboratory Procedures and Reports

The majority of all hospital laboratories as well as the independent clinical laboratories are called upon but rarely to run determinations for lead in the urine or the blood. Their equipment is inadequate for such determinations, and usually their technicians are untrained in these techniques. To rely upon such may lead to errors. Only the experienced laboratory should be utilized.

Errors also reside in the method of collecting samples and the type of containers in which they are collected. Another source of error is the laboratory report in which the decimal point may be typographically misplaced. The decimal point should always be suspect.

As to the basophilic or stippled cell count it has, in my opinion, little diagnostic value and the inexperienced physician should ignore its use. In the hands of a few physicians who conduct a frequent periodic check-up of their workers and who have trained technicians, it has a value in detecting impending intoxication. Basophilic stippling as done by the ordinary laboratory technician is too often completely unreliable.

Finally, as far as the laboratory report is concerned, what is the interpretation of "normal values"? This depends, to paraphrase the *New Yorker,* upon which author one reads. For reasons not apparent to me it is almost universally accepted by the laboratory that the upper limit of normal lead in blood is 0.05 mg/100 ml. Yet there are a number of authorities who feel that individuals with no exposure to lead may have a blood lead of 0.07 mg or 0.08 mg. It is unrealistic to hold normal values of either urinary or blood lead to a rigid figure. Most of the profession still believe that a slight upward variation means lead intoxication. The day before this paper was dictated a physician called the speaker and informed him that he had a patient whose blood lead was "grossly abnormal." Her blood lead was 0.06 mg, she had no exposure to lead and her symptoms did not fit into the picture of lead intoxication. From such interpretations are errors made.

Treatment Prior to Diagnosis

The advent of calcium disodium versenate has induced in some areas the use of this therapy prior to securing blood or urine for lead determinations. The error inherent in this type of procedure is obvious.

Summary and Conclusions

Still to be heard or read is the statement that plumbism is a protean disease. The tense of the verb should be changed to read — was a protean disease. Factors which once permitted months or years of exposure to undue concentrations of lead dust or fumes no longer exist. It would be extremely rare in the experience of any physician today to see an industrially induced case of plumbism characterized by the neuromuscular syndrome or encephalitis. It is therefore erroneous to assign to modern day lead intoxication the bizarre findings perpetuated in the literature.

Errors in the diagnosis of plumbism arise out of an inadequate history, insufficient knowledge of the occupational environment and reliance upon laboratories whose experience and efficiency are not known. A common source of error arises out of faulty collection of materials as well as the interpretation of reports submitted by the laboratory. The figures presented by the report must be evaluated in relation to the history of exposure and the clinical picture. It is my conclusion that plumbism is not difficult to diagnose if these common errors are avoided.

DISCUSSION

DR. L. E. HAMLIN: For those associated with occupations where lead is used, a good medical preventive program will demand that physicians obtain all the facts, especially a history of occupational exposure, and also differentiate lead intoxication from ordinary diseases. For example, in my own experience I can recall three such instances within the last few years. These occurred in a brass foundry where operations in the past have resulted in employees being exposed to fairly high concentrations of lead oxide. In each case symptoms that might accompany definite lead intoxication were present. However, when we checked the urine and blood over a considerable period of time and correlated the findings with atmospheric concentrations of lead, we found that the diagnosis of lead intoxication was not justified. In cooperation with our local physician, a man interested in lead intoxication, we were able to suggest that further investigations were necessary and as a result, the three cases were hospitalized for a period of two weeks during which time extensive studies

were completed. The final diagnoses were in one instance, chronic spastic constipation, in another liver abscess, and in the third case pellagra.

As I indicated, all these employees were men who had worked for a number of years in a plant where there had been considerable exposure to lead and it would have been reasonable to attribute their illnesses to lead intoxication had it not been for the intelligent use of Maximal Allowable Concentration Standards and the analytical procedures we adopted several years ago. I think this experience illustrates quite well the importance of what Dr. Johnstone has emphasized, namely the proper use of these laboratory methods. In our own lead control program we would find it exceedingly difficult to do without them. On the other hand, it is important to remember what Dr. Kehoe and some of the other speakers stated this morning about the place of MAC's, to the effect that at best they must be used only as guides, along with other pertinent facts, in making a diagnosis.

In this connection we should not overlook the fact that most industries, particularly those with well defined medical and hygiene programs, have people on their executive staffs who are quite conversant with MAC's and who take a pretty intelligent view of such standards. The standpoint of management is sometimes not too altruistic in this sense and may be a little selfish. A liberalized MAC may be used as an excuse to escape installing some necessary but expensive exhaust ventilating equipment. This is particularly true in times of recession such as we have gone through recently, so that, as Dr. Johnstone has said, the importance of making a proper diagnosis becomes all the more apparent.

One thing I should like to mention in this reference concerns the hospitalization and further study of cases such as the three that I have described. The fact that industry willingly accepted the cost of having these people hospitalized demonstrated a commendable attitude on the part of management. It was something that was not compulsory nor was it undertaken simply from the standpoint of avoiding medicolegal claims. The action was taken rather in the best interests of the employees' health.

Dr. Johnstone brought out another idea which I thought was very timely, and that was the importance of physicians getting firsthand information on all patients where occupational illness may be involved. In my opinion it is rather a sad commentary on our present system of medical education that graduating physicians know so little about industrial medicine. I realize that some steps have been taken to correct the situation but there is still a lot of room for improvement. I fail to see how any physician can possibly make an intelligent diagnosis of plumbism until he has some concept of what goes on inside a plant. A physician who takes time out from his busy practice to make plant visits is appreciated not only by management, in most instances, but also by employees who consequently have much more confidence in the recommendations he makes.

DR. C. H. HINE: I would appreciate a comment on the question of recurrence of lead intoxication in a person who has once suffered this after having changed to a second industry. I would like, specifically, to mention my own difficulty with a man who has had lead intoxication, who is now employed in an industry where there is no exposure to lead, but who has recurrent attacks of arthralgia and myalgia accompanied by an elevation of his lead excretion to the neighborhood of approximately .15 mg per 24 hours. He also has occasional gastritis and enteritis. Would you please enlighten me as to whether this is compatible with the recurrent intoxication?

DR. JOHNSTONE: When did he have the exposure?

DR. HINE: Approximately a year ago, and he is still having recurrent difficulties. He has had no re-exposure to lead, and I can not find associated with these reoccurrences any changes in his physiology which would account for lead mobilization.

DR. JOHNSTONE: I don't think he is suffering at all, one year later, from anything due to that lead exposure. I can't understand why you have .15 mg of lead now if he is not in that exposure. There is something faulty someplace. In my opinion, rather in my own practice, we remove the man from the exposure. I haven't hospitalized a case in many years, and I rarely treat them with anything other than iron for anemia. I believe most of the cases I see are mild enough that the physiological release of lead excretion takes care of that. If he is somewhat anemic, I put him on iron, and then he is checked in two weeks, four weeks, and in six weeks' time he is given a blood lead, and if his blood lead is normal, he returns to work, to the same environment if that environment has been corrected.

I can't understand your case. I don't believe that arthralgia and those things last a year after he has been relieved of his exposure. There must have been something way above and outside of what we normally see today. He could have had arthralgia at the time of exposure to lead. He has gotten lead from someplace else. You must have a good laboratory that you can trust.

DR. HAMLIN: May I ask how long the man worked and how many years he was exposed to lead?

DR. HINE: For approximately two years prior to this time, he was in the lead industry.

DR. JOHNSTONE: What kind of industry?

DR. HINE: I think he was engaged in the manufacture of lead batteries.

He had a case that was disputed, heard before the Commission, and awarded. I don't think, from the evidence presented at the hearing, there was any question but that he had a frank lead intoxication. He persisted to have a low grade anemia from this and also, on one trial of Versene, excreted large quantities of lead.

From my own experience, I am not sure how high a lead should be excreted in a normal individual. I think this person put out something like 3 mg to 4 mg in 24 hours.

DR. HAMLIN: I would agree with Dr. Johnstone. With this type of exposure you would certainly

have to look for some other factor to account for the employee's illness, particularly after the length of time he had been away from work. In our experience we have seen several men who have been subjected to high lead exposure for possibly 35 years, continue working without ever having had a recognizable episode of acute intoxication. However, as they have approached the age of retirement they have displayed symptoms. I can recall one individual who developed a case of what was thought to be intestinal obstruction but which turned out to be paralyticus ileus. The man underwent an exploratory operation from which he made an uneventful recovery but never seemed to be able to get rid of his lead entirely. It seems logical that lead stored in the body tissues over the years might eventually produce symptoms of intoxication in certain cases even after removal from exposure.

DR. HARRIET L. HARDY: Dr. Johnstone, I think, would be disappointed in me if I didn't take issue with him. My experience in the 10 years I have been interested in, and searching for, lead poisoning suggests that plumbism has by no means disappeared. I have seen some very dramatic clinical pictures which I think are admitted to hospitals mimicking other diseases and the term diagnosis is missed. I have seen two cases of jaundice from red cell destruction whose lead exposure was well substantiated with Dr. Elkins' help. I have seen a bilateral wristdrop in the case of a house painter who got well when he was removed from exposure and given several courses of intravenous EDTA. I have seen hematological abnormalities with long periods of disability. I have a hunch that the physicians that miss the diagnosis of lead poisoning are not here today. They are the house officers, and they are the internists who haven't yet had teaching in the field of occupational medicine.

Dr. Mayers and I were talking at lunch today about our repeated hope that the house officers, probably more than the medical students, would learn some of the criteria for diagnosis of plumbism that you and I take for granted, and which are common knowledge. Personally, I am convinced there is still a good deal of interesting, true lead-induced pathological change in our midst.

DR. PAUL REZNIKOFF: Just as the general physician or the internist fails to go into the industrial history of a patient, so the industrial physician very often fails to consider the entire medical picture of the patient. For example, we have had six since January, 1958, working in a garage, and they are subjected to lead inhalation. They are examined for some condition such as upper respiratory infection, and the physician finds they have a lot of stippling, and he makes a diagnosis of lead poisoning on the basis of that and some laboratory results which he thinks are a little off color. As a matter of fact, when they are thoroughly examined, we find they are individuals who have Mediterranean parents or grandparents, that they have a perfectly clear-cut case of Mediterranean anemia of the minor type. They do have a relatively low hemoglobin which doesn't bother them, and a lot of stippling, and furthermore we prove by a starch, gel electrophoresis examination that they have increased hemoglobin A2.

Those people are labeled forever lead poisoning because of stippling, because some laboratory gave them a report of a slightly high blood or urinary lead content.

I think it is important, therefore, to emphasize the fact that the industrial physician has to obtain a complete history and do a thorough physical examination and think of medical conditions other than an industrial disease because these are much more common in a workman than industrial disorders.

DR. J. C. AUB: In lead poisoning, you might get prolonged symptoms if you have bone disease which liberates calcium more rapidly than normal. Two of those would be hyperthyroidism and Paget's disease, a disease which comes at about the time these men get lead poisoning and which is missed unless you take a lot of x-rays.

DR. J. H. FOULGER: Dr. Johnstone has emphasized one important fact in this whole field of chemicals and ill health, the lack of skill of physicians as cross-examiners. Medical cases do not go to litigation where there is a clean-cut diagnosis. They go to litigation when the physician attending the plaintiff does not find it possible to make an ordinary type of diagnosis. Then he relies upon history, and of course, history is based on symptomatology. We have been so long sold on the old pathology idea that a specific disease is due to a specific etiological factor and gives a specific morphological pathological picture that we don't realize we are no longer in that era.

The symptomatology of the incipient effect of exposure to a hazardous chemical is no different from the symptomatology of many other ordinary diseases. Bacterial infections are chemical poisoning, not an eating away of tissue by bacteria. Even some forms of cancer in which the cancer invades the metabolic aspect of neighboring tissues can be a chemical poisoning. The symptomatology is due to interference with the fundamental cellular processes in the body; interference with key enzymes, those involving oxidation reduction situations, sugar metabolism, the liberation of energy for activity of muscles, the building up of proteins as I mentioned this morning in Borsock's work. So long as these diagnoses are not clean-cut and are made on poorly developed histories and poorly developed symptomatology, just so long will we have this type of case.

DR. RUTHERFORD T. JOHNSTONE: In industry, as you know, encephalitis from ingestion of lead is no problem. I want someone in this audience to explain to me why children, by ingestion, get encephalitis.

Our trouble in industry, of course, has been by inhalation. We have the reversible things, you understand. The second question I would like to ask is, in what kind of case is it felt necessary to use EDTA?

J. J. CHISOLM, JR.: Dr. Johnstone, the excretion

of lead in the feces of these children ranges as high as 100 mg of lead per day. This is five to 50 times the values reported for industrial types of exposure. The increased incidence of acute encephalopathy in children as compared with adults depends, at least in part, upon their more intense lead exposure.

DR. D. H. BYERS: I haven't measured nearly as many cases as Dr. Chisolm. It certainly is true in the few chips I have measured that I have seen children eat. It is quite obvious the exposure is enormous. Whether the child's greater inefficiency of pH control and chemical homeostasis adds to the hazard or not, I don't know. I had a sort of feeling it did. I think the exposure factor must be the most important one of all.

DR. H. D. SMITH: I, too, would favor that this is a dose factor primarily. We see some of the levels of lead in the blood are very high as well. Chisolm has already described the stool findings, and such intense exposure is apparent in the slide I showed on the child that died.

I don't think the susceptibilty is particularly a factor in terms of the central nervous system of children. We do see a collection of diseases involving the neurological system where age probably is a factor because myelinization of the central nervous system hasn't occurred until the latter part of the first year, but myelinization is pretty well completed by the time the child gets to the age when lead poisoning occurs.

DR. HARRIET HARDY: I was wondering if Dr. Smith could tell us what amount of lead was in the brain tissue of that autopsy of the child and other autopsied children. I am still interested in the idea there is some is some difference between the adult and the child in what the central nervous system does in response to toxic insult.

DR. SMITH: No, I am embarrassed. I don't have it on that individual's slide and still haven't found the exact figure. I just have it from Dr. Kehoe. It was high in this individual child. In others, though, we have found that if there is less than .3 mg of lead per 100 gm of brain tissue, even though clinically someone has said there are indications of lead encephalopathy, Dr. Kehoe has been very hesitant to make this diagnosis, and on each occasion when he has been in that position of differing with those of us who were the clinicians, our pathologist has found another cause for death.

There have been several examples of this, and I think they point out that even though there was a considerable amount of lead in the blood and in some of the other tissues, this was a coincidental finding in association with a disease which was itself fatal.

You asked this morning how our pathologist picked up this diagnosis. There are a couple of things that make him suspicious. In almost any case where there was evidence of acute cerebral edema and brain stem herniation, our pathologists have done two things: one, looked at the liver and kidney for the inclusion bodies that Blackman described a good many years back, and secondly, they have sent the brain or parts of the brain to the Kettering Laboratory for their confirmation by tissue analysis. The inclusion bodies are something that only make us suspect that this child has absorbed excessive amounts of lead. They don't prove the diagnosis of the encephalopathy. That requires the further step of cerebral tissue analysis for lead contents.

DR. HARDY: In other words, this is a nonspecific cerebral edema having demonstrated exposure to lead by inclusion bodies or its presence in tissue. It then remains for someone to take the bold step and say they belong together.

I think it is perfectly possible that children with varying degrees of cerebral edema might have quite serious morbid change and physiologic change disturbance in intelligence quotient or perhaps go blind, if they had lived.

I am interested in what causes the patient to die, and whether it is related to lead in the brain of adults as well as in children.

I remember so well discussing a case of a Negro maintenance man in the storage battery plant who had had good, solid exposure and was found dead in his bed in his home. Question mark — lead poisoning. There were staggering amounts of lead in the brain. In the discussion, I was the only one who was willing to put his death and the findings of lead in the brain together.

How much do you want to say that cerebral edema is lead related? See what I am getting at? I am suggesting that the cause of death could have been heart failure, or excessive administration of fluids, but when does one say this is lead poisoning and lead induced death? I am not saying it well, but I am trying to get at the problem of being so hesitant to say that lead is doing damage because you don't have as many pieces as you want in the equation.

DR. BYERS: I am afraid I can't straighten you out. Certainly when children die who have clinical pathological lead encephalopathy, they die with brain stem compression. They die with slowing respiration, pulse rate and blood pressure, anuria, all the usual evidences of increased cranial pressure.

I can't believe that this isn't in some way related to interference with the brain enzyme systems through amounts of lead which may not in themselves be impressive.

We haven't as many analyses, I am sure, as Smith has, but again you find amounts of lead which are rather above the usual run in these children. We try very hard to find other causes for death. We certainly look for other diseases at autopsy and don't find them.

DR. HARDY: Could we bring it back to this original point of the difference between the adult and the child brain in its response to lead as a possible factor?

DR. BYERS: I think one factor that I can't tie in very well at this point of the argument, and which is often not appreciated, is the growth factor. I originally got interested in lead because of children who had had lead poisoning and had been sent home from the hospital as cured, then turned up in my neurological clinic because they were mis-

behaving in one way or another, or not learning in school. One kid set the schoolroom on fire, another nice little girl danced around on the desk. None of these children had acute fulminating encephalitis. They all had evidence of lead poisoning like stipple cells, some increase in spinal fluid, total protein, GI symptoms, coproporphyrin in the urine, things of that sort.

At that time we didn't know about the importance of separating them from lead. We tried in a desultory way to separate them. Maybe we weren't successful about that.

The point I am trying to make about these children is that, though none of them had an acute encephalopathy at two or three years with their acute intoxication, when they reached six and seven they showed evidence of brain injury, and I think that many children get chronic encephalopathy from lead as well as this acute business. I think it is a question of degree where one merges into the other.

Now with treatment with EDTA and with protection from lead, we don't see that picture as often as we used to. In fact, we don't see it at all in the last five or six years.

This group of children deteriorates gradually without ever having had any acute lead encephalitis, and, therefore, I think that lead does something to the growing brain which is differeent from the adult brain. I don't know that I can prove it, but certainly it acts that way to me. That is all I am trying to say.

DR. HARDY: Perhaps, if we had enough specimens of adult and child brains in lead poisoned individuals, and knew enough about their clinical course, we might be able to say this. I do not think it is just an impression on your part.

DR. BYERS: To try to relate it only to the myelinization doesn't make sense, because the brain is multiplying a lot of things that you cannot demonstrate histologically, still changing after myelinization has terminated. Brain weight increases long after you can't demonstrate any change in your tissue histologically, and brain growth continues up to 17 or 18 years of age.

DR. HARDY: We have done a few electroencephalograms in adults with well established lead poisoning that nobody doubted, and there were changes on the electroencephalograms which reversed without any complaints from the patients as to headache. No one could see anything wrong with the eye grounds. I think lead is a real neurotoxin all right, and the threshold of production of symptoms from the lead varies enormously from patient to patient.

Now what Red really got up here for was to find out when we treat a case of lead poisoning in industry with EDTA.

It seems to me that you want the diagnosis established.

DR. JOHNSTONE: The diagnosis is established, but what induces one to give EDTA?

DR. HARDY: Yes. Well, the things that induce me to give EDTA are symptoms very hard to evaluate because they are subjective, meaning chronic constipation, abdominal pain, complaint of fatigue. What I want in the way of laboratory evidence is, if possible, some environmental knowledge. I usually can get this with Hervey Elkins' help, but if I can't have that, I want a lead urine above at least .5 mg per liter, and I want a porphyrin that is up.

We get quantitative ones in Boston from both the Massachusetts Division of Occupational Hygiene and the Massachusetts General Hospital, but let's have it at three or four plus in the terminology that we have been using, and in addition hematologic abnormalities and specifically some indications that there has been either disturbance in hemoglobin synthesis or actual red blood cells destruction.

This is gained simply by an iron deficiency anemia or the more elaborate studies of hemolytic effect such as changes in fragility of the red cells. Those are the things I want before I treat a case with calcium sodium EDTA.

I have some hesitation about using this material in patients I don't know well. I now do kidney function study, especially in older workers with long-time exposure, because my current opinion is that we have been much too casual about the effect of lead on the kidney.

I was excited by Dr. Chisolm's remark that they have been able to demonstrate renal tubular troubles and phosphate holding effects in children who have a lot of lead insult. I certainly have a small number of men who have had long term exposure to lead who do show evidence of renal damage.

If you put that together with what Harry Foreman showed in experimental animals, what the Swiss have shown and various other people, that if you give the right dose and give it rapidly as Laslo shows, you get damage in the kidneys as a result of EDTA administration. EDTA must not be used in patients with evidence of renal disease.

I think another factor that leads to the decision to use EDTA in a practical way is whether the worker — patient with lead poisoning — can forever after be free from lead exposure. If, for all the reasons all of us know, he may have to go back to lead even under the best industrial hygiene circumstances and the best will in the world, this seems to be an appropriate use for calcium EDTA if you can keep the man under medical supervision. I have had a couple of supervisors in storage battery plants who have been hospitalized with not too devastating lead poisoning, and nobody would challenge the diagnosis, but they have got to go back, and on occasions they have got a new worker on the pasting machines. They must see about the ventilation. They have a lot of reasons for putting their breathing zone above safe limits of lead. Such people, I believe, may be submitted to one to four short courses of calcium sodium EDTA therapy by vein unless they are suffering from some renal damage.

The other type of patients that present problems are those with uncertain diagnoses of lead poisoning and these we have already discussed. I have no hesitation in repeating courses of EDTA by

vein over and over again for short periods at low dosage with attention to laboratory studies of renal function.

I don't think such treatment carries a hazard if it is given slowly in three, four or five hours timed doses of the order of 1 gm to 2 gm depending on the weight of the man.

DR. JOHNSTONE: Am I entirely wrong, and do I jeopardize the future of this patient by treating him as I do, by merely withdrawing him from the environment? My daughters always said that all I know about therapy is to put a band-aid on the guy if there is something wrong on the outside and give aspirin if something is wrong on the inside. That is about the way I treat lead poisoning. Am I wrong withdrawing the man from exposure, and treating as I described in my paper? Is the future of that man jeopardized in any way by not giving him EDTA? Is it justifiable to put in a hospital a so-called minor case, running up expenses of giving him EDTA? In other words, is this whole philosophy of doing what we did before wrong, believing physiological excretion was the fundamental thing, and should we go over this EDTA almost routinely, eliminating the things you say about the kidney?

DR. HARDY: I certainly think that if a man has been exposed for 10 or 15 years steadily to the inhalation of lead, some of it above the so-called safe limits, and if this is reflected in his blood findings, he can be said to have had intoxication. Each case is a case by itself, and anybody that suggests that EDTA be used routinely is, in my opinion, in error.

DR. THOMAS SHIPMAN: I want to agree with the things that Harriet has just said. In the early flush of our enthusiasm for using EDTA in treatment for various kinds of poisoning, there has been something of a tendency to play the numbers game. It is quite encouraging to see the excretion of lead or plutonium increased by a factor of 10 or 20 or 50, and everyone in the hospital stands around and cheers when these numbers come out.

The fact remains, I think, that perhaps we have made only a very small impression on the total body burden. This comes back to what Dr. Johnstone just said. Is he damaging the patient's chances by failure to give EDTA? I don't think so. I think as far as lead is concerned, the great value of EDTA is in the relief of symptoms, and tiding the patient over a temporary rough spot.

I would add one other very small point. Harriet mentioned that Harry Foreman demonstrated the kidney damage in animals. He demonstrated it in animals after we had already demonstrated it on a human, a case that was quite well worked up and the story was published.

DR. W. C. WILENTZ: I am glad that Dr. Johnstone made some mention about the kind of a case where you would use EDTA.

There is one thing sure about the point of its use prophylactically, which was brought out here today, and that is, that by giving EDTA you can produce a sense of false security. There is no question about it, and anything that will do that must be used cautiously.

What I have been interested in observing here today, and yesterday, was the question "What has happened to our calcium therapy?" I am sure that is what Dr. Belknap had in mind.

I have heard Dr. Shipman talk about relief of symptoms of lead poisoning, in the use of EDTA. Did you ever see anything so spectacular in your life as the relief of symptoms from giving intravenous calcium therapy?

It is incredible. Nothing else has ever been manufactured that can give you that rapid, spectacular relief from symptoms. We have used calcium for years. There is no therapy that I know of that has been proved to be better than the old-fashioned calcium intravenous therapy.

Our results show it over the years. I have 75 to 80 lead intoxication cases right now. You can see my point of view. I am personally, from my own experience, still against deleading. I feel that it is safer, and more feasible, to let the deleading process take its natural course after you have gotten through with the acute stage.

I don't state that you can just ignore these men that are exposed. Somebody got the idea here that we are not treating these people. These doctors that spoke today didn't want to give anybody the idea they are not treating these men when they say they are permitting them to excrete the lead naturally. I am sure none of these doctors meant that, because you do treat them in your own particular fashion. And you get wonderful results.

I am still against deleading from what I have heard, particularly after what I have heard, and read, about EDTA.

I would like to ask one question of you, Dr. Hardy. Do you people in Massachusetts go entirely on porphyrin testing as to whether a man has lead poisoning or serious lead exposure? That is what I have been informed.

DR. HARDY: We are very much impressed with the level of porphyrin excretion in the urine as an index of the intoxication, not the exposure. That is the point. If you have a whole group of people in the storage battery plant who show a wide spectrum of lead values in urine, the porphyrin, we have found, when done quantitatively gives a good idea as to who is going to turn up in the sick bay. I would like to quarrel with you about the use of calcium as therapy.

DR. WILENTZ: Porphyrin, of course, is not on the program, but I know men who work in lead plants that have large porphyrin excretions and have never gotten sick. Of course, I am only talking about porphyrin cases, where everything else is within normal limits.

DR. HARDY: I think we have come to a very good area of disagreement.

DR. WILENTZ: We have records to substantiate this fact.

DR. HARDY: A good healthy area. This is the area where we need more investigation. I challenge the concept that it is all right to let me walk around with indices of pathologic physiology which is what a high porphyrin is, whatever it is, because if it is

due to alcohol as Dr. Rezinkoff was saying yesterday and which has been shown years ago, then maybe something has to happen about that, but if you get it with low hemoglobin and you know the lead exposure. . . .

DR. WILENTZ: That is different.

DR. HARDY: That is?

DR. WILENTZ: That is different. That isn't what I asked you. If you get high porphyrin excretions with other lead signs and symptoms, that is a different story. I can show you three or four dozen cases of high porphyrins, which we observed, that had no indications of symptoms or signs of lead intoxication. I am not talking about low hemoglobin, low blood counts or high stippling cases.

DR. HARDY: You and I would have to set up the standards of lead intoxication so there is mutual agreement. My quarrel with you on calcium therapy rests on the fact that calcium forces the lead into the bony skeleton rather than out of the body. And, since there is a limit to the amount of lead that the skeleton can hold unless the man is permanently removed from lead exposure, the risk of lead poisoning is increased. Am I not correct that forcing lead into the bone with calcium is the basis for its use as therapy?

DR. WILENTZ: Right.

DR. HARDY: The ionic lead goes into some form of phosphate and disappears in the. . . .

DR. WILENTZ: Mobilizes! Mobilizes the lead within the bony structure, and takes the lead out of circulation, thus giving the body a chance to take a "breather" and prepare for the next stage, which is the excretion of lead by normal, natural metabolic and physiologic processes.

DR. HARDY: Dr. Johnstone wants to join.

DR. JOHNSTONE: I think, Harriet, you know a damn sight more about this than I do.

DR. HARDY: I do not!

DR. JOHNSTONE: I think actually the only value I found in calcium is, it relieves the gastrointestinal spasm, the metabolism. Don't forget that.

DR. HARDY: Our friend was saying he would rather use calcium and put the lead back in the bones. I am quarreling with that. I think we want the lead out.

DR. WILENTZ: It is excreted naturally thereafter, in a simple, painless and efficient process.

DR. HARDY: Do we take the man off the job?

DR. WILENTZ: There are not so many, not if your plant is really doing a job. You remove men when you have to, and watch the others as a precaution.

DR. HARDY: But in structural steel painters, for instance, there are many lead exposures where it is not simple to control the hazard.

We are discussing a very complicated problem, and that is why, as you say, there is no easy prophylaxis, no routine handling, but each case is studied and treated as it occurs.

MR. CARL WALTERS: I would like to ask Dr. Hardy if, with intravenous injections of the EDTA, she has been able to keep the injections low enough in content to permit men to continue to work, or must they be hospitalized or taken off the job?

DR. HARDY: We insist on taking them off the job, for study of renal function and intravenous treatment with EDTA.

MR. WALTERS: I know of some doctors who are dispensing the EDTA tablets orally and permit the employee to continue working, but someone said yesterday they didn't approve of it.

Do you approve of the oral administration of EDTA?

DR. HARDY: No. The effects, both good and bad, are not understood. Absorption through the gut of lead combined with EDTA is a possibility. Nobody really understands this. Maybe some lead gets into the blood as it comes through the intestinal wall.

Dr. Miller gave the same opinion for adult lead poisoning. Dr. Smith agreed for the children, and I hold the same view.

DR. BYERS: I spoke of this impressive demonstration of what EDTA given by mouth, with lead in the gut, does, and I think it is worth repeating.

We had a kid come in with mild lead poisoning whose blood lead level we didn't get measured, but who had a fairly high coproporphyrinuria, about 250 to 300 micrograms per day, had stipple cells, had spinal fluid total protein of 80. Quite conscious. His lead output was measured for 24 hours; around 200 micrograms per 24 hours. At the end of this period by mistake he was given two tablets of EDTA by mouth.

DR. HARDY: Half gram?

DR. BYERS: Half gram tablets, one six hours after the other. Within 24 hours he was putting out 1,500 micrograms of lead per 24 hours in his urine. His spinal fluid total protein had gone up to 400. He was unconscious and in convulsions and his coproporphyrin went way up beyond what we could measure.

We then put him on intravenous EDTA and things calmed down, but he has been permanently damaged by this. That is, he has damage which was not reversible, to the brain. I think this drug should never be given by mouth.

The other thing I would like to point out is that before we got into this mess we were fussing with oral EDTA in children who had been treated because of lead poisoning mostly with encephalitis, and we had gotten about a dozen children and we were sure we had eliminated the lead from their homes. We put half of them on oral EDTA, a gram a day. The other half we left alone. No treatment at all, and just following the urine qualitatively, seeing them in the hospital once in two weeks, doing a qualitative test for coproporphyrin, this group of childrens' coproporphyrin stayed positive anywhere from four to 17 months. These are the ones off oral EDTA.

The ones on EDTA ran coproporphyrins from four to 16 months, and certainly we didn't get rid of any more of the lead from them by this oral use of the drug, so that the oral use of the drug is ineffective as well as dangerous.

A LAWYER LOOKS AT LEAD

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I am simply going to call your attention to some of the responsibilities that rest upon the manufacturers and producers of lead because you are dealing with a toxic substance. There are two particular features that I would like to discuss briefly — one, your liability to the employees who may be exposed to the hazards of lead poisoning, if I may use that term, because that is the way it is described in our compensation statutes; and secondly, to the consuming public. I know those matters have been touched upon by prior speakers, and I simply want to call one or two particular points to your attention.

First, with respect to your employees, or the employees who become exposed to the hazard of lead in your operations. You all know that now compensation statutes are effective in all states of the union, in all federal jurisdictions, and by that method we have removed from the field of common law litigation disputes that may arise between the employer and the employee. In a word, these compensation statutes impose upon the employer the liability as an insurer for those particular matters that have been made the subject of compensation in the statutes.

Your laws are not uniform. They differ with respect to coverage. They differ with respect to the type of injuries that are made compensable. They differ with respect to the requirements of insurance, the benefits that are payable and the administrative agencies that are charged with the administration of the laws, but behind them all there is one common purpose, to provide prompt compensation at the time that the injured employee really needs it for those injuries that are truly compensable under the given statute.

Originally, as you know, they were designed to compensate for accidental injuries. Little by little they have been amended to provide compensation for occupational diseases, and today there are only two states, Mississippi and Wyoming, wherein occupational diseases are not compensable. Again we do not find uniformity with respect to that particular feature because in some states we still have the schedule system, naming the particular disease that is compensable; lead poisoning, for example. Some states don't even provide that. In other states, we have the so-called general coverage laws, and may I make this comment that with respect to the administration of those laws, our commissions and our courts are coming to treat these laws as health insurance laws whether employers or manufacturers like it or not, and I for one don't like it. They are treating them as health insurance laws and you can get Dr. A, who will testify in a very limited and superficial manner that John Smith, claimant, has a particular occupational disease, and you can get your Red Johnstones and Lloyd Hamlins and Lem McGees and Bob Kehoes and all the rest of the specialists in the field of occupational diseases. I should not have omitted my friend, Tony Lanza because he has testified for me, too, but you get the one statement by some one doctor that John Smith has the occupational disease and in spite of all the testimony — perhaps that isn't a fair statement — but in spite of the weight of the testimony, our commissions are coming to find, and our courts are sustaining that finding, that if there is evidence in the record that the claimant has a disease for which claim has been filed, then an award is made. So those of us in practice for insurance carriers, self-insurers for industry, when we step up to the trial tables, have more than two strikes against us in the defense of that type of claim.

I do not mean to belittle the need for the compensation statutes. Some of you who are present here have heard me say before, and I now repeat, that if we are going to treat these laws as health insurance laws, let's call them health insurance laws. Let's stop this business of calling them workmen's compensation laws. That in my mind has become a misnomer.

Certainly one thing is true. With respect to your employees, they are justly demanding a safe place in which to work, safe tools with which to work, protection from the hazards of their employment. Furthermore, they are properly and justly demanding compensation for injuries sustained in your employment.

I say to you that in your role as employers there is a definite responsibility to see that those objectives are attained, and in this enlightened age I do not believe that any one will disagree with that statement. If you show me the executive who concerns himself about the health and the welfare of his employees, I will show to you the company whose compensation risk and cost are minimum.

It is simply good business on the part of you employers to see that the health of your workmen is properly protected.

I would like to call your attention to these legal definitions that have grown up with respect to the term "injury," because after all, we are now compensating for injuries under the compensation statutes.

There have developed three distinct concepts with respect to injury. First, the inability to earn full wages. That is what we started out with because the statutes pay a percentage of the wage that the employee was earning at the time that the injury occurred. Secondly, the total inability to perform any further work. In other words, total disability. Third, the event of an employee becoming actually incapacitated from performing work in the last occupation in which he was employed. In the administration of these compensation laws they are being treated as damage statutes.

John Smith comes in and has a complaint, and that complaint is not resolved in the best medical opinion. It is based upon the fact that he, John Smith, is a poor employee. The person or the corporation against whom he files his claim is a corporation and has assets, and therefore recovery should be had by him.

"Simple service, simply given," that is what your employees are giving, and I say to you and perhaps it is needless to say, reappraise your relationship to your employees and see that they are properly protected in the particular job that you give to them to do.

Now may I say just a word with respect to the liability to the consuming public? Here, since I had not intended to get into detailed discussion of a matter that has already been developed, I will simply touch upon as it relates to these labeling statutes.

Only recently the Committee on Toxicology of the American Medical Association has recommended the enactment of a uniform Hazardous Substances Act in the several states. Some states have already adopted that particular Act. I don't think we want more laws. I think we need proper administration of the laws that we now have. Are we going to have a federal law dealing with the subject of labeling? Are we going to have 49 state laws dealing with that subject? Are we going to have countless municipal ordinances and regulations relating to hazardous substances?

A hiatus will result; confusion to industry We have to label this particular product in one manner if we sell it in the City of New York. We have to label it in another manner if we sell it in the City of Baltimore, and so forth. We could go on ad infinitum.

The lack of uniformity with respect to that is a real problem in my judgment. Perhaps I shouldn't tell this. Perhaps I tell it incorrectly. The Baltimore Commissioner of Health was talking to me with great pride about a recent statute, an ordinance in the City of Baltimore dealing with labeling. The City Department of Health is going to send to every child that becomes four months old, a copy of this ordinance with the substance of the ordinance, and it is felt that this will protect or prevent lead poisoning.

Unfortunately, the mother or the father who gets it and reads it will not properly understand it when you speak of a toxic substance, and no matter what their understanding may be they are still going to use the product.

The moral that I mean to develop from that is to caution the members of this Association as to the responsibility that is imposed upon them by the various states, by the various municipal ordinances that have been and are becoming affected dealing with this particular subject.

If you don't, we will get common lawsuits based upon negligence which are tried in courts before juries. There is no ceiling to the limit that that jury may return as the verdict against Company A, B or C, and therefore you may well face the most distressing litigation in our common law courts that you can imagine.

DISCUSSION

MR. ARTHUR S. JOHNSON: I want to make this general observation as background material. It is either by good luck or good underwriting or good engineering services that the American Mutual has experienced only 12 alleged lead poisoning cases during the last 10 years. Nine of these were nondisabling, requiring only medical treatment of a few visits to a doctor and very simple medical care. Of the three disabling cases, one was an exposure to some melted lead by a man who seemed rather more sensitive than others. He was not seriously ill, and the compensation payment didn't amount to much.

The second was a welder or acetylene burner, working on some painted steel and this involved a few weeks of disability. Incidentally, I am startled that nobody talked about cutting up painted steel with acetylene torches. It is really one of the prolific sources of lead poisoning. The scrap

industry is just cluttered up with it. The final case was an interesting one from the legal point of view. It was an exposure to the hazards in a smelting and refining company. The man had intermittent exposure and very brief exposure. By brief I mean he walked across the premises, but he had nothing to do with lead or lead fumes as such. Exposure was considered insufficient to produce his condition, but the Industrial Commission found in favor, because it was demonstrated that he did have lead poisoning. Their statement was that it is prima facie evidence of occupational disease.

It is the understatement of the day that the compensation laws of the several states are not uniform. If anything could be more chaotic, I can't imagine what it might be. Ted Waters spoke of the compensation laws providing exclusive remedy. Exclusive remedy, I think, is against the employer, and Ted would be the last to suggest that it was exclusive to the extent that no third party action was available.

The favorite sport today, if the laws of the state permit it, is to take compensation, let the compensation carrier subrogate his interest in that amount of money and go after a third party such as the general contractor, another contractor or a supplier under the principle of products liability, which to all intents and purposes has made the injured employee public.

A little word or two about the liberalization of the laws by extending benefits. The concept of injuries being compensable under the statutes had a serious spurt during the inflationary period of the last half dozen years. This bears upon this law of indemnity as opposed to the law of negligence. It used to be that three or four or five thousand dollars would settle almost any case, but one hundred or one hundred fifty thousand dollars is common today in these cases. There seems to be some evidence, however, that with the inflationary period plateauing off, the value of money leveling off, it might be safe to predict that the cost of claims would kind of plateau off a little, too.

I was interested in Ted's statement that the original concept of accident had evolved first to encompass the inability to earn wages due to a personal injury arising out of and in the course of employment, and he had two or three categories of development there. It might be a little too simple.

There still remains considerable difference between the personal injury notion as such and the disability as such. I need to labor this a little bit because we may be coming in to a period when disability as a measure of loss of earnings or inability to work goes by the board, and the mere fact of personal injury becomes the criterion.

Let's take the popular topic of the present time, deafness alleged to arise out of and during the course of industrial exposure.

The notions vary between the several states that are now playing with that problem, whether the deafness must have accompanying it a disability as measured by a loss of earnings, or deafness as a personal injury in which deafness gets paid compensation. This question of loss of earnings has always been a tough one. For instance, a case of asbestosis a number of years ago was judged to be a permanent and total disability and was compensated as such under the compensation law of the state. The man immediately got another job, still occupies it in apparently good health, and his earnings are in excess of any he earned at the asbestos plant.

I would like to amplify what Mr. Waters has said with respect to management not intending to give lip service by promulgating a procedure and then forgetting it. His remark was that those who established control of lead as an operating policy get their money back many fold.

Let me express it in just a little different way. It is the intention of our insurance company to be quite willing to insure concerns against the accidents and injuries that might be described as the unforeseen events that arise out of operating the business, but to insure business risks, or to insure the inevitable foregone conclusion of lead poisoning cases arising out of flagrant failure to provide a safe place to work is quite outside of our underwriting policy.

It might be helpful to wind up my comments on Waters' paper with this one. It seems to me that it might be well to establish the three criteria which must be met to establish compensability of a case of lead poisoning for which the employer may be responsible under the compensation law. I refer to the legal aspect as it now is understood, not this fantastic one of merely compensating injury.

First, there must be established the fact that the man has lead poisoning, not something else. Second, that there was a lead poisoning hazard to which the man was exposed, that he didn't get it somewhere else, and finally that he has been disabled by the injury or the disease of lead poisoning. That is looking at the classic principle that his disease was sufficient to reduce earning power.

Those are the three approaches that our claim-legal people undertake to follow, and the criteria by which they try to establish whether they have a defense of a case or whether the injured employee should be compensated without further ado.

DR. JOSEPH C. AUB: Talking as we have today about lead poisoning gives the impression that it is a common disease. This is hardly fair in this case where the disease has become less frequent and less severe. Much has been learned about this disease, and this knowledge is really being applied more to its prevention than to accurate diagnosis and therapy. Improvements have occurred in all categories.

This is as it should be. Because the disease can be handled more intelligently, we must be careful not to discuss it as though it is more prevalent than its real incidence justifies. I think the discussion today has tended to give that impression.

Effects of Season and Temperature on

CHILDHOOD PLUMBISM

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Review of Literature

The Baltimore City Health Department[1] has shown that lead poisoning in children has a marked seasonal distribution with almost all of the cases occurring between the months of May and October. Most of the cases in the Baltimore study were diagnosed by pediatricians in various Baltimore hospitals on the basis of clinical symptoms plus a blood level above the normal range, determined by the Health Department's blood lead analytical service. In addition, a field worker from the Health Department visited the homes to determine the source of the lead and to obtain samples of the incriminated material for analysis. Of the 720 cases which the Health Department investigated between 1931 and 1958, the majority occurred among children between one and three years of age and were attributed to pica associated with the ingestion of lead paint. The children came chiefly from families in the lower economic classes who resided in old houses where the interior wood and plaster has been coated with lead paint. This seasonal distribution, which is shown in Figure 1, has occurred every year without exception since the investigation began.

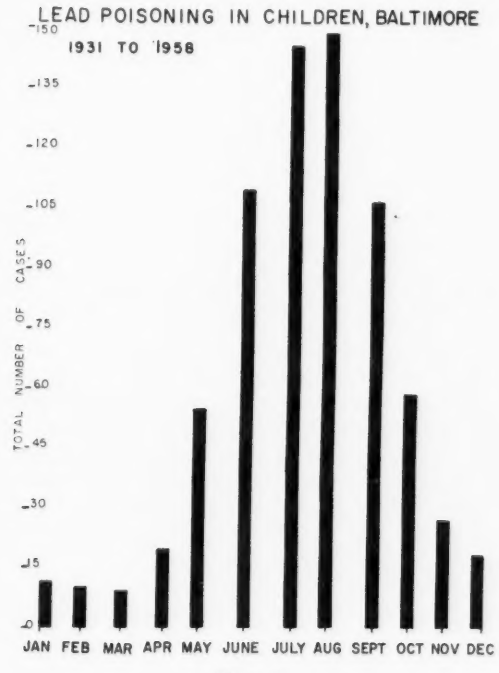

Figure 1

A similar seasonal distribution has been reported for 246 cases in St. Louis,[2] 143 cases in New York,[3] 30 cases in Philadelphia[4] and 21 cases in Chicago.[5] Also, Blackman[6] quotes several Japanese authors as mentioning a tendency of lead encephalitis to appear during the summer and early fall in their country.

In a recent study of childhood lead poisoning, partly supported by the Lead Industries Association, Chisolm[7] showed that although the children reached the ambulatory and teething age at all seasons of the year and thus could be potentially exposed to lead ingestion, the acute encephalopathy did not develop in any of his 32 cases until the first summer following a three-month period of potential lead ingestion. Thus it would seem that the chronic ingestion of lead is precipitated into an acute episode by some factor associated with summer.

In adults this seasonal pattern of lead poisoning is not evident, probably because of the many varying factors which affect adults. Kehoe[8,9] found no accumulation of lead during the summer in his experimental subjects on a high lead intake. Although the concentration of lead in the urine was high in the summer, the total urine lead excretion decreased in association with the decrease in urine volume. The occurrence of stippled erythrocytes increased in summer. On the contrary, Holmquist[10] noted a lower level

of stippled erythrocytes in lead exposed individuals in summer. Hammond[11] reported a sharp increase in the concentration of lead in the urine of lead exposed workers during extremely hot weather. Since adjustment was made for specific gravity, this increase could not be attributed to a more concentrated urine. Horiuchi and Takada[12] showed that normal healthy persons have a higher blood lead concentration in summer than in winter. Shiels[13] noted a lower incidence of occupational lead poisoning in summer than in winter in various industries in Melbourne and ascribed this distribution to an increase in lead excretion in sweat during the summer. On the other hand, when he investigated the occurrence of occupational lead poisoning in relation to climate, he found that in persons who were excreting .3 mg lead or more per liter of urine, the percentage who had clinical symptoms of lead poisoning was greater the warmer the climate. Thus the data fail to show any clear-cut trend in adult lead poisoning with season.

The seasonal distribution of lead poisoning in children has been attributed to various factors. Exposure to the more intense ultraviolet radiation from the sun in the summer and the resulting increase in vitamin D has been the factor most prominently implicated. Shelling and Hooper[14] suggested this theory on the basis that vitamin D increases the absorption of lead from the intestines if the diet contains a high calcium-low phosphorous ratio. Rapoport and Rubin[4] tested this theory in experiments on rats. Animals which were fed a diet containing lead and were exposed to the sun or given supplementary doses of vitamin D daily, lost weight, became ill or died, whereas those given lead but kept in the dark without added vitamin D showed only retardation of growth. Added support is given to this ultraviolet radiation factor by the close parallel between the seasonal distribution of cases and the monthly variation in the intensity of antirachitic radiation from the sun in temperate climates.[15]

Although the increase in ultraviolet radiation may account for the summer peak in childhood lead cases, there are some reasons to doubt that it is the only factor involved. This theory depends on the assumption that these children have a low phosphorous diet and/or lack a normal amount of vitamin D in their diet. Although vitamin D increases the absorption of lead from the gut, Sobel and his co-workers[16] showed that vitamin D had no very marked effect on the concentration of lead in the blood if the diet contained a high phosphorous-low calcium ratio. With prepared milk fortified with vitamin D so widely used by lower income families as a major source of food for their children, a lack of sufficient vitamin D and a low phosphorous intake would not be expected. Furthermore, under some conditions vitamin D increases the deposition of the lead in the bones.

Another explanation which has been suggested to explain this seasonal distribution is that children have more opportunity in summer to chew exterior paints, which generally contain more lead than interior paints. However, data from the Baltimore Health Department surveys indicated that indoor objects are the chief sources of the lead ingested.

The other important environmental condition which has been suggested as the factor responsible for the seasonal distribution of these acute lead poisoning cases in children is the increase in environmental temperature during the summer months. Just as in the case of ultraviolet radiation, the monthly distribution of cases in Baltimore follows very closely the monthly maximum temperature curve. A few investigators have reported an increased susceptibility of animals to some drugs and chemicals with exposure to high environmental temperatures or with a rise in body temperature,[17,18] but only three papers have been found which relate this factor to lead. Blackman[6] showed that rabbits which were subjected to 37°C following a seven-week period of subcutaneous injections of lead, died within 102 hours, whereas those similarly injected but kept at room temperature survived, as did control rabbits at 37°C. The body temperature of rabbits at 37°C rose 3° or 4°C. A seasonal variation in the susceptibility of rabbits to subcutaneous injections of lead was found by Germuth, et al,[19] the average survival time being much shorter in summer than in winter. On the other hand, Rapoport and Rubin[4] reported that the exposure of rats, which had been fed a high lead diet, to 40°C, four hours per day had no apparent effect of the animals in spite of a rise in rectal temperature of 1° to 2°C.

Experiments on Effects of Temperature on Susceptibility of Laboratory Animals to Lead Poisoning*

Because the ultraviolet radiation theory did not seem an adequate explanation of the seasonal distribution of these childhood cases and because of the few and conflicting experimental data on the effect of environmental temperature on lead poisoning, a series of experiments was undertaken in this laboratory to study the effects of environmental temperature and humidity on the susceptibility of laboratory animals to lead poisoning.

Mice were used in most of these experiments

*This investigation was supported by Research Grant RG-4505 from the U.S. Public Health Service. Part of the experiments reported in this paper were performed by Miss Sheila Joardar.[20]

although rats were tested occasionally to confirm the results on the mice. The two temperature conditions studied were 72°F with approximately 50% relative humidity as the normal exposure and 95°F as the high temperature exposure. In some cases the humidity was kept low in the high temperature chamber but in most of the experiments a humidity of 85% was used. The body temperature of the mice varied considerably in both environments, but the rectal temperature of the mice in the hot chambers did not average more than 1.5°C above those in the normal exposure. In the initial experiments groups of 10 to 20 mice were exposed continuously to the two temperatures for three days before and 14 days after injection with lead. They were injected either intraperitoneally or intravenously with a single dose of lead acetate or nitrate sufficient to cause death in approximately 20% to 40% of the mice at 72°F. In every experiment control mice were maintained at each of the test temperatures. They were injected with sodium acetate or nitrate in amounts so that the acetate or nitrate concentration was equivalent to that in the lead dose. The mice at the 95°F temperature were compared with the mice at 72°F in regard to total mortality during a two-week post injection period; latent period, i.e., time between injection and first death; and the average survival time, i.e., the time between injection and death in the fatal cases. The time of death was taken as the midpoint between the time when the animal was last observed as living and the time when it was found dead. Each experiment was repeated several times and the data were combined for statistical treatment in order to determine if the differences were significant.

The exposure of the mice to the high temperature increased the mortality significantly, hastened the onset of deaths and accelerated the rate of dying. The effects were more marked when the lead was injected intravenously than when injected intraperitoneally. Since the same results were obtained with intravenous injections as with intraperitoneal injections, the increased susceptibility to lead at the high temperature cannot be attributed to a more rapid absorption of lead from the peritoneal cavity.

The duration of exposure preceding injection of the lead was varied in a series of experiments. High temperature had the same effect whether the mice were exposed only one day before injection or for longer periods up to 30 days, showing that no acclimatization occurred during this period. However, the effect was greater if the exposure to the high temperature began immediately after injection of the lead than when the exposure preceded the injection.

Since children may be exposed to hot days and cooler nights, several experiments were performed in which the mice were exposed to the high temperature for only eight hours each day. The effects of the high temperature were much less under these conditions than when the exposure was continuous. This result may explain why Rapoport and Rubin found no effect of high temperature on lead poisoning in their animals which were exposed to the high temperature for only four hours per day.

In most of the experiments a high humidity was associated with the high temperature. In a few experiments the effects of lead injection were compared in mice kept at 95°F 85% RH with those kept at 95°F 25% RH. The results indicated that humidity was much less important than the dry bulb temperature. This result was not surprising since mice do not sweat.

Because children sweat in high temperature and may become dehydrated, it seemed possible that the seasonal distribution of childhood cases might be attributed to dehydration rather than to the high temperature. Since mice do not sweat like man, dehydration was produced by restricting water intake leading to a 12% loss of body weight over a three-day period preceding the injection of lead and was maintained for three days after injection. Dehydration significantly increased the mortality at both test temperatures and hastened the onset of deaths at high temperature when the lead was injected intraperitoneally, but had less effect when it was injected intravenously.

After determining that high environmental temperature increased the susceptibility of mice to acute lead poisoning, a series of experiments was performed to study the effect of high temperature on chronic lead poisoning. These chronic experiments probably duplicate more closely the conditions existing in the childhood cases. In these experiments the mice were injected intraperitoneally six days per week with smaller doses of lead nitrate than those used for the acute experiments. Control mice received comparable doses of the sodium nitrate. The mice were kept at normal temperature during the injection period. The injections were continued until the lead group showed a consistent weight loss which was usually between 16 and 26 days after the beginning of the injections. Half of the experimental and control mice were then placed in the high temperature chamber. The mortality was significantly higher and the latent time significantly shorter in the lead injected mice exposed to the high temperature than in those kept continuously at the 72°F temperature.

The physiological mechanism responsible for

the higher mortality and the more rapid onset of illness and death in the mice and rats at the higher temperature is not clear. A number of possibilities can be suggested. The increase in body temperature may have increased the rate of chemical reactions in the mice and thus increased the reaction to lead, but the magnitude of the temperature effect was considerably greater than would be expected on the basis of the small rise in body temperature and the usual Q_{10} value of two to three which is characteristic for most chemical reactions in the body. The basal metabolic rate in the mice probably was increased by exposure to the high temperature. Experiments are now in progress to determine if an increase in metabolic rate produced by thyroxine increases the susceptibility of mice to lead. Since the mice at high temperature eat less food and tend to lose some weight, it was thought that these factors might contribute to their greater susceptibility to lead, but experiments performed by McQuary[21] in this laboratory showed that restriction of food intake did not increase susceptibility to lead poisoning. It seemed probable that the mice at the high temperature might be excreting less lead than those at normal temperature. This theory was tested by comparing the urine and fecal lead excretion in rats at 72°F and 95°F temperature. The determinations showed that the animals at the high temperature excreted significantly less lead in their urine over a period of 14 days following the intravenous injection of lead than the animals kept at 72°F. The decrease in the output of lead in the urine was probably related to the lower total urine volume since Kehoe[9] showed that the urinary lead output per unit of time varied in accordance with the volume of water excreted by the kidneys. The total fecal output of lead was also somewhat less at the high temperature. A number of other experiments are currently in progress to test various other theories which might account for the increase in susceptibility of mice to lead poisoning at high temperature. It is hoped that these experiments will help to explain the seasonal distribution of childhood cases.

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DISCUSSION

DR. J. J. CHISOLM, JR.: Under Dr. Baetjer's experimental conditions, heat and dehydration certainly do enhance the toxicity of lead. Her experimental conditions require comment in order to determine to what extent this data may be applied to clinical situations. The degree of dehydration produced experimentally in the mice was quite severe; namely, a loss of water equivalent to 12% of body weight. Such severe states of dehydration may nonspecifically enhance the toxicity of a number of agents. This severe degree of dehydration is rarely encountered clinically in acute lead intoxication. I should be most interested to know what lesser degrees of dehydration may produce in future experiments.

With respect to the temperature elevation produced in the mice I understand that mice are relatively poikilothermic. Human infants greater than three months of age do not exhibit wide fluctuations of body temperature in response to change in environmental temperature as do the mice. Children with acute lead intoxication have normal temperatures unless they experience excessive vomiting or prolonged convulsive activity as a result of their acute lead encephalopathy.

I call your attention to Dr. Baetjer's observation that continuous exposure to high environmental temperature increased lead toxicity in the mice to a much greater degree than did intermittent exposure to high temperature. Differences in heat exposure may explain some of the differences between the results of various workers who have studied this problem.

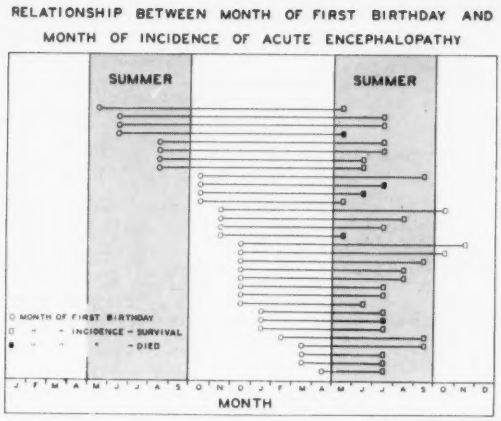
RELATIONSHIP BETWEEN MONTH OF FIRST BIRTHDAY AND
MONTH OF INCIDENCE OF ACUTE ENCEPHALOPATHY
SUMMER
SUMMER
MONTH OF FIRST BIRTHDAY
INCIDENCE - SURVIVAL
DIED
J F M A M J J A S O N D J F M A M J J A S O N D
MONTH

Figure 2

Relationship between month of first birthday and month of incidence of acute encephalopathy.

In this graph the month of onset of acute symptoms for each of the 32 patients who developed acute lead encephalopathy prior to 2 years of age is shown on the right. On the left is the month of the child's first birthday. These points are joined by a bar. The length of each bar, therefore, represents the assumed duration of lead exposure (in months) for each child. Twelve months of age was selected as the average age of ambulation. The nature of the exposure in this series required that the child be ambulatory in order to reach the sources of lead in his environment. In this manner a relation between presumed duration of exposure to lead and the seasonal factor in the production of symptoms can be demonstrated. (reprinted from *Pediatrics* 18:950, 1956)

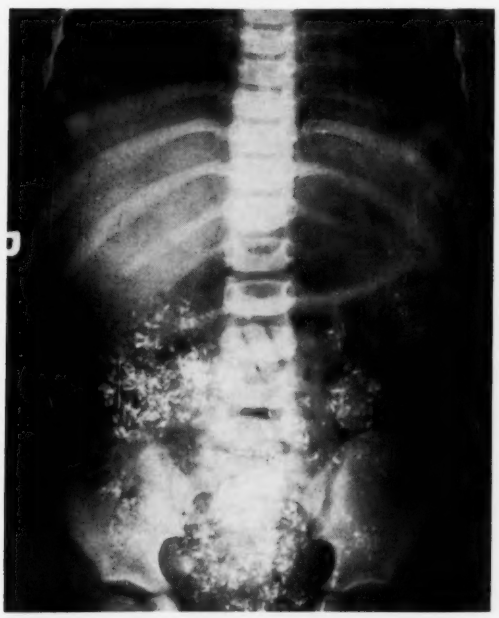

Figure 3

Abdominal x-ray shows large numbers of paint flakes eaten by child. Flaking paint in the home which this child was eating contained >5% of lead upon analysis. Six weeks after removal from lead exposure blood lead concentration had decreased from 0.33 to 0.14 mg. lead/100 gm. blood. No specific therapy was given. The child remained clinically well.

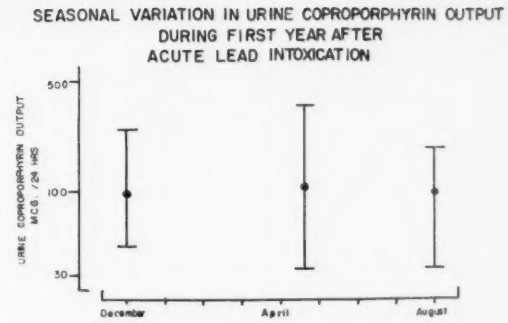

Figure 4

Seasonal variation in urine coproporphyrin output during first year after acute lead intoxication.

This graph shows the mean and range of serial 24 hour urine coproporphyrin outputs in a group of 15 patients. They had had acute lead encephalopathy during the summer preceding the winter, spring and summer included in this graph. None was ingesting lead during the period of time shown in the graph. All had increased bony stores of lead. Urine coproporphyrin output is used as an index of biochemical lead toxicity. Under these conditions no seasonal fluctuation in urine coproporphyrin output is observed.

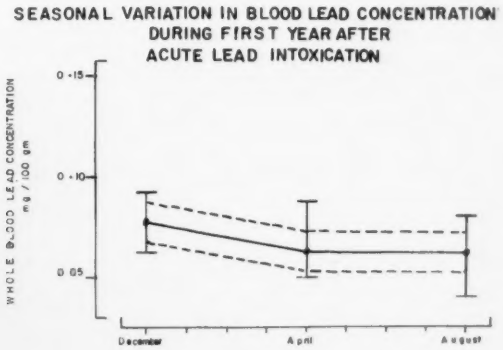

Figure 5

Seasonal variation in blood lead concentration during first year after acute lead intoxication.

This graph shows the changes with respect to season in mean and range of serial blood lead concentrations in the same group of 15 patients for which data is presented in Figure 3. The environmental conditions are the same. No seasonal fluctuation can be seen; rather, a gradual diminution in blood lead concentration is apparent.

How do these experimental observations parallel clinical experience in children? They simulate a situation that is occasionally met in children who develop chronic infections superimposed upon an increased body burden of lead. After a prolonged period of continuous fever the acute manifestations of lead intoxication may develop in such a child irrespective of the season of the year. The older clinical literature is replete with such examples. Since the advent of antibiotics, chronic febrile illnesses have become rare in children. Acute lead poisoning pre-

TABLE I.

DAILY FECAL EXCRETION OF LEAD IN CHILDREN BEFORE AND AFTER REMOVAL OF ENVIRONMENTAL SOURCES OF LEAD*

Classification of Patients+	No. of Patients	No. of Specimens	Lead Output (mg./24 hrs.) Mean	Median	Range
Types II and III					
At Home During Exposure	6	10	44.0	27.0	5.04 - 104.0
In Hospital after Therapy	5	13	0.360	0.240	0.062 - 0.850
Types I, II and III					
At Home After Exposure	8	15	0.565	0.511	0.039 - 1.50
Type I					
At Home During Exposure	5	12	2.16	1.11	0.116 - 9.60
Household Controls					
At Home During Exposure	11	23	0.832	0.651	0.087 - 1.93

*The household-study group has been divided according to both diagnostic classification and presence or absence of lead exposure, in order that the observed differences in fecal excretion of lead under these varying conditions can be seen. Each specimen represents a 2 to 4 day pooled collection of feces from the lead content of which is calculated the milligrams lead excreted per 24 hours. An average of two such specimens were collected from each patient during each period of observation relative to exposure.

+Clinical Diagnosis at time of Admission to Hospital:
Type I—asymptomatic increased lead absorption
Type II—acute lead intoxication
Type III—acute lead encephalopathy
(adapted from *Pediatrics* 18:946, 1956)

cipitated in this manner has likewise become rare.

Dr. Baetjer designed her experiments to bypass the role of intestinal absorption. Clinically, this is a most important factor. Acute lead intoxication occurs almost exclusively during the summer in children *actively* eating lead. The only recognized exception to this is the presence of febrile illness just discussed. I will present some data to illustrate this important clinical point. Those data in Table I were obtained from a group of children all of whom were excreting increased amounts of lead in the feces. You will note that the children who became ill were those who were eating the larger amounts of lead at the time of their illness. When they returned to their homes but were no longer eating lead no recurrence of acute plumbism resulted although they were still exposed to the high environmental temperatures of the summer. This abdominal x-ray film (Figure 3) represents a belly full of paint and plaster. The child's blood lead concentration about the 1st of July was .33 mg per 100 gm of blood. Although asymptomatic he was hospitalized to prevent further lead ingestion. He never became ill. We attribute a large part of the improvement in our "therapeutic results" to removal of patients from exposure prior to the onset of symptoms. Such patients are exposed during the remainder of the summer to high environmental temperature and increased ultraviolet solar irradiation, but they do not become acutely ill.

The studies of Sobel[1] and of Rubin and Rapoport[2] indicate that vitamin D plays an important role regardless of the diet in increasing the absorption of lead from the intestine. Sobel and his co-workers also showed that diets producing a low concentration of phosphorus in the serum tended to increase the concentration of lead in the blood. It is of interest that children severely ill with acute lead intoxication do have a low serum phosphorus concentration, apparently as a result of the renal tubular lesion produced by lead.

Finally, I should like to present some observations on the effect of season on children not eating lead. These data were obtained from children who had had acute lead encephalopathy during one summer and were followed during the ensuing winter, spring, and summer with serial measurements of blood lead concentration, urinary coproporphyrin output, and hematologic parameters. These children had an increased store of lead in the body. Figure 4 suggests that urinary coproporphyrin output in this group of 15 children was not affected by season. Figure 5 indicates that a gradual diminution in blood lead concentration occurred independent of season in this same group of children. We concluded from these data that season has little effect upon children not actively ingesting lead.

Studies on the effect of heat, of vitamin D intake and of solar irradiation explain much about the increased clinical incidence of acute lead encephalopathy during the summer months. They do not offer a completely satisfactory explanation for the mechanism by which encephalopathy is produced. There are other possible explanations. One almost totally uninvestigated possibility is the effect of ultraviolet radiation upon porphyrin metabolism. Porphyrin metabolism is grossly deranged in lead intoxication. I should think this offers still another fruitful field for study.

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DR. J. H. FOULGER: I was particularly interested by your last remark, Doctor, about porphyrin metabolism. There is a complete parallel to this situation in poisoning by methyl methacrylate monomer. This substance, in high concentration, interferes seriously with the porphyrin metabolism in animals and produces coproporphyrinuria, and those animals when exposed to ultraviolet light die at a greater rate than in the dark. It is an easy way to produce

a porphyrinuria because the compound itself is not very highly toxic. It does affect the liver, so also to some extent does lead.

Of course, the question of temperature and dehydration and increased metabolic rate is not new. One of our greatest fears in the use of DDT and the possible absorption of DDT by children was that DDT is stored in the fatty tissues including the brain, and an increased metabolic rate from a fever incidental to thermal effects or to disease will mobilize the DDT in the bloodstream, causing acute DDT poisoning and death so you have those two parallels to this lead situation.

It doesn't follow that the cases represent acute poisoning in the summer. That curve, though it looks like a probability curve, may merely be similar to transient in electrical engineeering. A steady process has been going on of absorption of lead. Suddenly something comes along that reverses that process.

Now the fundamental process, if we can accept porphyrinuria as being a very early sign of exposure to lead, may well be the process I was talking about, the interference with incorporation of amino acids and similar compounds into the cells and the accompanying energy factors involved there.

We are dealing with an encephalitis irritation of the central nervous system. The enzyme system of the brain is based particularly upon the oxidation-reduction mechanisms, and the basic material on which the brain feeds is glucose. If one interferes with these systems involved in oxidation and reduction, and certainly the hemoglobin and porphyrin system is one of them, we are seriously endangering the life of an animal or a patient.

DR. HUNTINGTON WILLIAMS: In Baltimore we have a record of more cases of child lead paint poisoning possibly than any other community, seven hundred twenty-four so far reported since we began this war in 1931. One hundred twenty-two of them have died. I saved my discussion on yesterday's papers and will put it all into a very few moments.

The New York City labeling requirement on lead paint was the first. It has been followed in Kansas and Illinois, but when we made ours up, we found we couldn't follow it because it was chiefly directed at places where children can chew. We worded it differently. In one tenement ceiling from which the paint is peeling and falling to the floor, the paint is 16% lead. I call it the stalactite room. A child picked up the flakes of paint, ate them, was made sick and was sent to Dr. Bradley's clinic. Both schools, Maryland and Johns Hopkins, are hard at work with us on this problem in Baltimore.

This house has now been posted as unfit for human habitation and the family is moving out into a housing project because it just isn't safe for that child to go back and keep chewing on this, so a labeling saying that you must not put it where a child can chew it would not cover this situation. A child can't chew off the ceiling. He chews off what is on the floor or on a window sill, usually.

I am sure you have run into this error in diagnosis. I consider the New York situation where a child of two died in 1951 of lead paint poisoning. She was taken to two different doctors and was diagnosed as a virus infection and so on. I see the clock running out on me, and then she was taken to four different hospitals and there was no diagnosis made. At death the medical examiner decided it was lead paint poisoning from eating paint flakes.

Childhood Cancer

Cancer is much more common among children than is generally realized, and currently causes about 4,000 deaths a year in the United States among children under 15 years of age, it is reported by statisticians of the Metropolitan Life Insurance Company. This is nearly 50 percent higher than the toll only a decade ago, reflecting in part the rapid growth of the child population.

In the 5-14 age group, cancer takes more lives than any other disease, accounting for one out of every four deaths from disease. The death rate from cancer in childhood is highest at the preschool ages, rising gradually to a peak between ages three and four. At each of the childhood ages, the rate among boys exceeds that among girls by one fifth.

Leukemia is the most common form of cancer in childhood, being responsible for nearly half the cancer death toll at ages under 15. Cancers of the nervous system — chiefly the brain — constitute the second most frequent category and account for about one fifth of all deaths from cancer in childhood. Other fairly frequent sites of childhood cancer are the kidney and bone.

Chemotherapy appears to offer great promise in the management of common childhood cancers. Some of the chemicals developed to date have been helpful in alleviating symptoms and prolonging the lives of children with leukemia. A large and intensive research program in cancer chemotherapy has been organized.

EDTA THERAPY

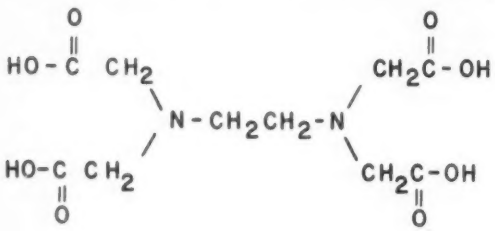
in Persons with Excessive Lead Absorption from Industrial Exposure

• LEE H. MILLER, M.D.
Kettering Laboratory
University of Cincinnati School of Medicine
Cincinnati, Ohio

Excessive lead absorption by persons in industry may occur as a result of one or more of the following circumstances: inadequacies or failures of existing measures for control of processes in which lead or lead compounds are used; poor personal hygiene; individual or group carelessness or indifference; unrecognized sources of exposure to lead; and accidental exposure to readily absorbed lead compounds such as tetraethyl lead.

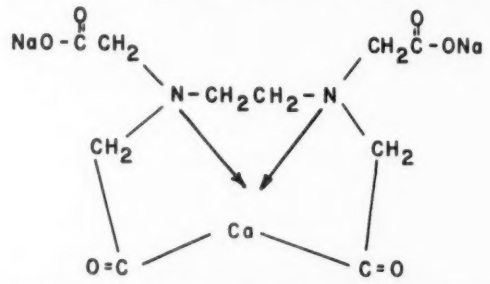
Because these circumstances still occur with surprising frequency, it is necessary that physicians who are responsible for the health of persons engaged in occupations in which there is exposure to lead, and those who undertake to treat persons suspected of having lead poisoning, be acquainted with a basic body of information that must include: (1) Familiarity with the symptomatology, physical findings, clinical laboratory findings and the natural clinical course of the syndrome. (2) A knowledge of the range of the concentration of lead in the blood and urine of persons who have had no unusual exposure to lead, and the significance of deviations from these values when obtained by reliable analytic methods performed by competent, qualified personnel. (3) Recognition of the fact that certain findings such as a gingival lead line, an increase in the numbers of "stippled" erythrocytes or elevated levels of lead in the blood or urine are not, by themselves, diagnostic of lead intoxication. (4) A practical understanding of the pharmacology of potentially useful therapeutic agents, the indications for their use, their limitations, possible harmful effects and misuse. Items 1, 2, and 3, have been discussed thoroughly elsewhere.[1,2,3]

Since the previous Lead Hygiene Conference, held in 1948, many fascinating contributions have been made in therapeutics. Notable among these has been the introduction and use of EDTA (ethylenediaminetetraacetic acid, Figure 1) and its salts, all of which are "chelating" drugs. Chelation is the term applied to the process



Edathamil (generic name)
Ethylenediaminetetraacetic acid
(Ethylenedinitrilo) tetraacetic acid

Figure 1



Edathamil calcium-disodium (generic name)
Calcium disodium salt of ethylenediaminetetraacetic acid
Calcium disodium salt of (ethylenedinitrilo) tetraacetic acid

Figure 2

whereby a ring-like structure is formed in which a special type of bonding (coordinate) takes place between some of the atoms that form the ring.[4] A multivalent positive ion such as lead or calcium, when incorporated in a ring complex or chelate, no longer retains its ionic properties. A sequestering agent is a compound that reacts with multivalent positive ions and retains them in an unionized state in a water-soluble product. EDTA and its mono and disodium salts, therefore, are both chelating and sequestering agents. When calcium is added, a chelate is formed; therefore, edathamil calcium-disodium (Figure 2) is the calcium chelate of the disodium salt of the acid, edathamil-EDTA.[5]

Pharmacology

The administration of EDTA or its mono or disodium salts to the animal organism results in the chelation and elimination of calcium. Because of this mechanism, it is not difficult to produce toxic manifestations with these agents.[6] To avoid the possibility of producing a state of hypocalcemia, edathamil calcium-disodium is used. The administration of this compound, in lieu of the acid or its mono or disodium salts, does not prevent the removal of lead from the body fluids, and indirectly, the soft tissues, since it proceeds to replace the calcium in the ring because of the greater stability of the lead EDTA complex. The newly formed lead complex is highly soluble in water. Since the lead in the chelate is bound firmly and is no longer in an ionized state, it does not exert its characteristic toxic effects. It is apparent at this point that these properties of edathamil calcium-disodium meet some of the specifications for a suitable or ideal therapeutic agent of this type; for example, the end product should be water soluble; it should be stable and not readily broken down by metabolic or other means within the body; it should be excreted rapidly; it should, for the sake of convenience, be effective when administered orally, and be readily absorbed; and finally, it should be relatively nontoxic when administered in effective amounts over prolonged periods of time. The latter includes the effects that might be induced by the depletion of trace metals that are necessary for the functioning of enzyme systems and other biologic mechanisms within the complex animal organism.

It has been demonstrated that edathamil calcium-disodium is quickly and widely dispersed throughout the soft tissues and fluids after intravenous or intramuscular administration, and that it is not concentrated significantly in any organ.[7] The compound does not appear to enter the cellular components of the blood, and the level in the spinal fluid is far below that found in the plasma.[8] After parenteral administration of the drug, excretion occurs rapidly, primarily via the kidneys. It was found that over 50% was eliminated from the body within the first hour, while 90% was removed within seven hours. The absorption of the drug from the alimentary tract is delayed and relatively poor. Evidence of renal damage has been observed in humans and degenerative changes in the tubules of the kidneys have been produced in animals when relatively large doses were administered over prolonged periods of time.[9,10]

The primary "deleading" action is apparently accomplished by removing the lead from the plasma and other body fluids. Shortly after the intravenous administration of a dose, the levels of lead in the blood may rise[11] without producing adverse effects. The lead level then falls, as excretion of the complex proceeds. Subsequently, the lead content of the blood may increase appreciably, and it may attain very nearly to its original high level, as the lead in the skeleton tends to come into equilibrium with the body fluids and indirectly with the soft tissues of the body. Following upon the administration of the chelating agent, the rate of lead excretion is increased greatly, reaching a peak soon, and then tapering off somewhat as the administration of the chelating agent is continued.

The recommended maximum dose for administration intravenously for each 10 pounds (4.5 kg) of body weight is 0.17 gm per hour, 0.33 gm per day, or 1.67 gm per week.[5] The drug should be given, in a concentration not to exceed 3%, in normal saline or in a 5% dextrose solution. The maximum dose per course of treatment is 2.5 gm for each 10 pounds (4.5 kg) of body weight. Courses should be separated by an interval of seven days, and it is inadvisable to exceed two courses, until or unless analytical results demonstrate a clear need for further therapy. Such need exists when the concentration of lead in the blood fails to diminish satisfactorily, or fails to remain well below a dangerous concentration. All persons undergoing therapy should be checked frequently for evidence of renal damage.

EDTA and the Prophylaxis of Lead Intoxication

The routine, frequent, or infrequent use of edathamil calcium-disodium, or other present or future drugs, as prophylaxis against the absorption of excessive quantities of lead cannot be condoned. As has always been true in the past, prophylaxis can be achieved safely only by controlling the sources of exposure to lead by the application of proper measures of industrial hygiene. The attitude that this cannot be accom-

plished generally in industrial operations reflects either ignorance of the true facts or an unwillingness to correct unsafe conditions (there are exceptions which result from the brevity of certain operations or the occurrence of unusual or unforeseen conditions). In the occasional circumstance where this is not practicable, strict adherence to recognized and properly supervised personal protective measures in conjunction with provision for adequate sanitary facilities, insistence upon good personal hygiene and sound medical supervision of the workers, will prevent the development of cases of lead intoxication.

Quite apart from the fundamental philosophy that prophylaxis should be attained by control of the environment, there are other valid reasons for not employing edathamil calcium-disodium as a preventive measure. First, the toxicologic potentials of the drug are not fully understood. The toxic effects observed in humans and animals from relatively short periods of administration have been mentioned; however, the effects that may be produced by the administration of even low doses over prolonged periods to humans are not known and are matters for conjecture. Second, since this drug is absorbed poorly from the gastrointestinal tract, it is unlikely that the additional quantities of lead that may be eliminated by its use would be sufficient to prevent illness when compared with the total amounts of lead that are absorbed and retained during exposure to potentially hazardous conditions. Third, the administration of the drug may mask the symptomatology of mild or early lead intoxication, thereby preventing the recognition of hazardous exposure before a more serious or prolonged illness is produced. Fourth, while under the effects of the drug and for variable periods of time thereafter, the levels of lead concentration in the blood and urine are meaningless and may be misleading for diagnostic and medicolegal purposes. Finally, the use of such agents, regardless of their efficacy, tends to lull those persons responsible for the health of the workers into a false sense of security which, invariably, is accompanied by a relaxation of recognized procedures and control measures. Such action, sooner or later, is bound to have serious consequences for all concerned.

Edathamil Calcium-disodium and Lead Intoxication

The objectives of therapy in all cases of lead intoxication are to treat the acute episode and to assist the individual to return to his optimum level of health in the shortest time possible. Paramount to both objectives is the immediate termination of exposure to lead. With edathamil calcium-disodium, it is now possible for short periods of time to effect safely the elimination of appreciably greater quantities of lead than heretofore.[12,13] While this is highly desirable, the extent to which this modifies the ultimate clinical course of the disease cannot be stated with certainty. Dramatic subjective improvement shortly after the institution of treatment has been reported in cases of poisoning from inorganic lead. In other cases, however, symptoms have persisted and have necessitated the employment of additional time-proved measures such as the administration of calcium gluconate intravenously for their relief. Other favorable responses, such as a sharp decrease in the numbers of "stippled" erythrocytes in the blood or in the concentration of coproporphyrin in the urine, have been reported frequently.[14] Some of the claims of subjective improvement in mild cases have been over enthusiastic in all probability, since it is known that this occurs quite frequently soon after withdrawal of the patient from the exposure. It has been noted by a number of observers that, following a course of treatment, the lead in the urine returns to levels of the same general order of magnitude as those found prior to treatment. This is not surprising since it has been shown, in carefully conducted long term experiments, that there is a definite relationship between the length of the exposure and the period of time over which increased amounts of lead will be excreted in the urine after the exposure has ceased.[15]

Edathamil calcium-disodium has been used in patients with tetraethyl lead intoxication.[16,17] As in the cases of intoxication produced by inorganic lead, the administration of the drug resulted in a definite increase in the excretion of lead in the urine. No definite significance could be attached to transient periods of clinical improvement that occurred in association with the increased elimination of lead, since periods of improvement and exacerbations are characteristic of that illness. It is of some importance, however, to note that no untoward effects of the application of this therapy have been observed.

In conclusion it may be stated that edathamil calcium-disodium is a drug that is capable of forming a chemically inert lead-complex that is rapidly eliminated from the body. At present, it is believed that the drug is most useful in the treatment of the acute phase of the illness. It is likely, however, that its principle virtue lies in its ability to expedite the elimination of potentially toxic quantities of lead from the body. By this means, one may hope to shorten the period of disability or of unemployment of the industrial workman. The body of knowledge concerning its useful application in cases of intoxication from lead and other metals is grow-

ing steadily, and it is hoped that its true value in the therapy of lead poisoning will soon be established.

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Discussions of Dr. Miller's article and of Dr. Smith's article appear on page 151, following Dr. Smith's paper.

Rice Farmers' Hazard Licked

When a laboratory scientist develops a new chemical compound, he can usually expect it to be noted in a scientific journal. Occasionally, if the discovery is important, he attains national recognition. Almost never, however, does it bring to him the veneration of a nation. Dr. Irwin B. Wilson, professor of Biochemistry at Columbia University, is an exception to the rule. In addition to the national recognition he received in the past two years for his success in designing "PAM," 100% effective nerve gas antidote, Dr. Wilson has been informed that he has gained the veneration of the people of Japan. The reason for the acclaim is PAM's dramatically effective results in treating Japanese rice farmers contaminated by parathion, a toxic chemical used in certain insecticides.

PAM has solved an occupational hazard that had plagued Japanese rice farmers for many years — the accidental poisoning from insecticides used in rice fields. In a country that depends heavily upon rice production for its national income and the use of insecticides as a control measure in rice paddies, the discovery is of paramount importance. In the five years before PAM was put on the market last May, there were 5620 poisoning cases.

In spite of the fact that PAM's effectiveness against parathion poisoning was generally recognized at the time of its announcement, Dr. Wilson was taken by surprise when he learned of its dramatic results in Japan. Soon after PAM became available in that country, letters began arriving at Columbia, telling of the compound's successful use in that country.

PAM is 2-pyridine aldoxime methiodide, a crystalline solid that dissolves in water to yield a clear yellow solution that is easily and inexpensively synthesized, and is nontoxic in amounts necessary to preserve life. In its use against major nerve gases, PAM has proved 100% effective in cases that had always been 100% fatal on test animals. PAM has not only proved by its success in Japan to be of widespread humanitarian value but it has opened new vistas of research into the future toward the understanding of the functioning of the nervous system and the development of chemical treatment of nervous disorders.

LEAD POISONING IN CHILDREN

and Its Therapy with EDTA

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Since lead poisoning among children is a consequence of the production and distribution by man of certain chemical products, theoretically it should be entirely preventable. Nevertheless, the illness continues to occur with devastating results. In Cincinnati, during the first 10 months of 1958, 20 instances of excessive absorption of lead by children were documented with four deaths reported. To introduce this topic and to show the fulminating consequences of the ingestion of lead, we shall relate the story of one of our recent patients.

Elaine C. had always appeared to be a pretty little girl with a big yellow bow in her hair and a full life before her until early in September, at age two and a half, she began to vomit, and became quite lethargic. After one day of these symptoms her alarmed parents took her to the Emergency Room of the Cincinnati General Hospital.

The physical examination demonstrated that Elaine was drowsy and markedly pale. Her liver and spleen were each slightly enlarged. A careful neurologic examination revealed only questionable increase in her reflexes. Sensitized by the knowledge of the high incidence of plumbism among children in Cincinnati during the preceding months, an alert resident physician proceeded to obtain a blood count and smear, a urinalysis and x-rays of the child's abdomen and wrists. While awaiting the results of these studies, he questioned Mrs. C. about Elaine's oral habits and obtained the history that ever since Elaine had learned to walk the previous fall, she had been chewing on bits of plaster pulled from a broken area of the kitchen wall. Although Mrs. C. had not thought this behavior to be harmful, she had tried quite vigorously, but fruitlessly, to arrest the habit.

When the results of the laboratory studies indicated a moderately severe anemia with basophilic stippling of the red cells, the presence of albumin, sugar and coproporphyrin in the urine, dense lines of radio opacity at the ends of the long bones of the forearm, and large amounts of radio opaque substances in the intestinal tract, a presumptive diagnosis of lead poisoning was made and the child was admitted to the pediatric ward shortly after midnight.

In order further to evaluate the possibility of lead encephalopathy a spinal puncture was performed and the cerebrospinal fluid was found to be under mildly increased pressure equal to 260 mm of water, but to contain no cells. Therapy was begun immediately. Enemas were given to remove as much lead-containing material as possible from the intestine, and therapy with calcium EDTA was started by slow intravenous infusion. It was 3:30 a.m. when the weary intern tumbled into bed, virtuously vain about his skill in aborting the ravages of pediatric lead poisoning. Alas, he did not sleep long, for at 6:15 a.m. he was notified that Elaine's breathing had become slow and irregular, with frequent periods of apnea. A check showed that her pupils were now dilated and unreactive and a repeat lumbar puncture revealed that the spinal fluid pressure had risen precipitously to 500 mm of water. It was obvious now that severe encephalopathy was present.

Following a hurried consultation with neurosurgeons, it was decided that the only hope of saving the girl's life rested upon immediate relief of the cerebral hypertension. Past experience had shown that the use of hypertonic glucose or sucrose solutions* brought only transient improvement followed by further increase in the brain swelling, and that efforts to relieve the pressure by means of repeated spinal punctures were both inadequate and fraught with serious risk of sudden death. Accordingly, with the hope

*To date we have not had any experience using 30% solutions of urea. In other centers considerable enthusiasm exists for this drug.

of decreasing cerebral tissue anoxia consequent to the encephalopathy, the child's temperature regulating center was paralyzed by pharmacologic methods and her body temperature lowered to 90°F. Thereafter, she was hurried to the operating room where a radical decompression of her brain was accomplished by the removal of almost all of her skull, except a narrow strip of bone down the center overlying the sagittal sinus. Prior to the operation, the child's breathing had become so infrequent that artificial respiration had been required throughout the operation and afterwards she was placed in a Drinker respirator. In addition to the previous therapy with Versene and hypothermia, anticholinergic drugs and a slow gastric drip of skimmed milk were initiated to prevent the development of a so-called "Cushing's Ulcer," and a constant bedside watch was begun. Nevertheless, four hours following the conclusion of surgery and only 20 hours after the child's arrival at the hospital, the heart beat ceased and she was declared dead. The results of the analytical studies for lead are recorded in Table I.

TABLE I.
POSTMORTEM TISSUE ANALYSES FOR LEAD

E. C. (C.G.H. #361-8-24)	
Blood	0.64 mgm Pb/100 Gm
Liver	3.81 mgm Pb/100 Gm
Vertebrae	14.90 mgm Pb/100 Gm
Feces	31.80 mgm Pb/100 Gm on ash

Were this an isolated or unusual case history our narrative might stop here, but regrettably this is still an all too typical picture. Some two weeks following Elaine's death, our clinicians and pathologists reviewed her case. We should like to report some of the conclusions brought out in their discussion.

As already mentioned, lead poisoning among children remains a serious menace. Its reported incidence in any locale reflects primarily the interest and awareness of physicians and the ready availability of analytical studies for lead. As an illustration of this fact, the graph (Figure 1) depicts the incidence of pediatric plumbism in Cincinnati, where we are indeed fortunate to have available the facilities of the Kettering Laboratory. It may be noted that during the years 1941 through 1948 only eight cases were diagnosed. In 1949 the incidence rose, but we were not yet alerted to the disease, for three of these eight cases had been erroneously thought to be poliomyelitis, and it was only upon postmortem examination that the correct diagnosis was made. This experience jarred us violently and, as can be seen, we soon found that the disease was quite prevalent.

Further evidence of the incidence of this disease was thrust upon us this past summer by the discovery of evidence of absorption of toxic amounts of lead as a coincidental finding in two children with other major disorders. In each instance some one clinical finding common to both plumbism and to the other disease led to the obtaining of blood for analysis for its lead content. Bradley and his colleagues[1] have similarly shown that many unrecognized cases of lead absorption in potentially toxic amounts exist in certain segments of the population. They obtained blood specimens from 333 children in clinics in the socioeconomically deprived sections of Baltimore and in 44.4% there was evidence of dangerous absorption of lead.

The map of Cincinnati (Figure 2) shows that a relatively small area of the city contributed almost all of the cases of lead poisoning between 1940 and 1957. The involved areas are the tenement sections. Furthermore, as urban redevelopment has forced the destruction of old homes in one area, the more recent cases have come from a region which, not too many years ago, fostered the four hundred. No new paint has been added to these homes; instead, the explanation for the appearance of saturnism is the fact that the paint has been allowed to crumble and peel; that less well informed families now live in the area, and that socioeconomic conditions frequently prevent sound child rearing. Thus, even though modern household paints may be essentially

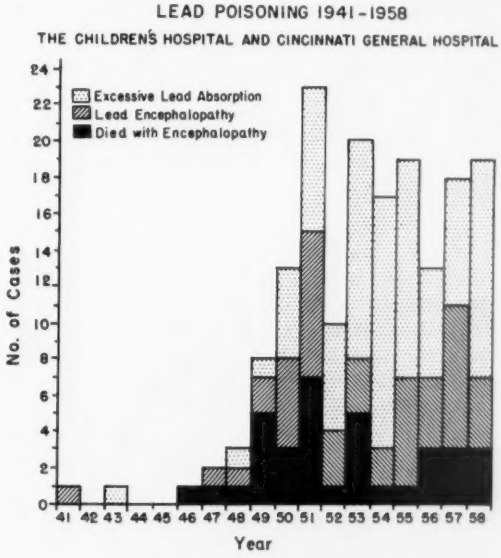

Figure 1
The incidence of lead poisoning, lead encephalopathy and death from lead poisoning seen at the Cincinnati Children's Hospital and the Cincinnati General Hospital 1941-1958.

Figure 2
A map of Cincinnati, Ohio, indicating the location of homes of pediatric patients with lead poisoning seen between 1940 and 1957. Of note is the intense concentration in the downtown basin area. Urban redevelopment in this district has resulted in the more recent cases coming from the region in the right center of the city.

lead-free, the threat of childhood lead poisoning will remain a public health problem for many years to come.

Before turning to therapy, we wish to stress a few of the clinical differences between childhood and adult plumbism. The typical findings in adults of peripheral neuritis, abdominal colic, and lead lines along the gums are all quite rare in children. Abdominal pain does occur with considerable frequency, but it is not so severe as to cause the child to double up or to have a board-like abdomen. Associated with the pain are intermittent vomiting, anorexia and constipation. The major concern of pediatricians is the high incidence of encephalopathy, which occurs in about one third of all childhood lead poisoning.

In the management of any child found to have absorbed potentially toxic amounts of lead, two problems must be faced regardless of the presence or absence of signs of actual intoxication: the immediate removal of as much lead from the soft tissues as possible, and the prevention of re-exposure to lead. For the former problem, calcium disodium EDTA or Versene is the accepted drug of choice, but therapy with it is far from ideal. Numerous studies have shown that the initial course of EDTA given intravenously removes only a small per cent of the total body lead and not even all the lead in the soft tissues. On the average, only 25 mgm of lead is cleared by the first course and four or five days time is required for this.[2] Accordingly, in most instances we give at least two courses of therapy and at times many more are needed before safe levels of lead in the blood ensue. Oral therapy for children seems unwise with rare exceptions, for not only is Versene by this route less effective in removing lead from the body,[3] but also it is frequently difficult to be certain that the child's exposure to lead has ended. A further problem we have met is the exacerbation of cerebral symptoms in the first 24 to 48 hours following the initiation of parenteral therapy with EDTA. To date, a change to the subcutaneous or intramuscular route of administration with efforts to limit the volume of fluid given has not resulted in a clear-cut improvement in our results. We are now recommending a more gradual onset of therapy, beginning with 25 mgm of EDTA per kg of body weight over the first 24 hours and then, if all goes well, increasing to 75 mgm per kg per 24 hours for four more days. It should be stressed that Versene is not a curative drug, but serves only to lower the amounts of lead in the body more rapidly than occurs by natural processes. Therefore, Versene alone cannot be considered as adequate therapy, especially for the more threatening manifestations of lead poisoning.

Efforts to prevent further exposure to lead are also confronted with difficulties, the major of these being that the causes for pica are not fully understood. To be sure, in many cases, psychiatric abnormalities in the child or disturbances in his environment can be uncovered[4] and because of these we routinely seek the assistance of our social service department. However, attitudes cannot be changed overnight and economic deprivation often defies correction. Although a moderately severe iron deficiency anemia is almost universally found, therapy with iron has not been of much value in aborting the pica, even though the anemia is relieved. Accordingly, as in other forms of lead poisoning, preventive efforts must be based upon removing the source of exposure. To this end, the labors of the health departments have been of considerable value once a case of plumbism has been reported. However, little has been done to correct dangerous situations before poisoning has occurred, in spite of our knowledge of the epidemiology of the disease.

When the disease has progressed to the encephalopathic stage, a real threat both to the brain and to life exists. The marked swelling of the myelin tissue within the rigid bounds of the skull results in extreme increases in intracranial pressure and in compression of the blood vessels supplying the brain. The integrity of the brain cells is thus threatened by anoxia, as well as by possible direct enzyme poisoning by the lead.[5] In an effort to decrease cerebral metabolism and thereby to minimize any cerebral metabolic deficit of oxygen or other nutrients, we

have, during the past 15 months, used hypothermia, maintaining the patient's temperature in the vicinity of 90°F to 91°F, through the use of ice packs plus pharmacological methods of paralyzing the temperature regulating centers. Despite therapeutic failures in several of our initial attempts with hypothermia and despite the fact that this form of treatment does increase the complexity of fluid therapy and may retard the removal of lead, we believe the procedure is sufficiently simple and carries adequate theoretical reasons for causing improved results to justify further trial.

When, in spite of other therapy, the cerebral spinal fluid pressure continues to rise and when dangerous consequences of such pressure develop, such as irregular respirations, apnea, marked bradycardia, papilledema or prolonged seizures, then radical cerebral decompression has been resorted to as a life-saving measure. The results reported by McLaurin and Nichols[6] (Table II)

TABLE II.
RESULTS OF THERAPY WITH RADICAL DECOMPRESSION*

	Encephalopathy	Died
Prior to decompression therapy	21	13 (62%)
Since decompression therapy:		
a) total	13	2 (15%)
b) treated by decompression	7	2 (29%)

*McLAURIN & NICHOLS: *Pediatrics* 20:653, 1957.

indicate a definite decrease in mortality following the introduction of this method of treatment, but unfortunately only life and not brain function appears to have been spared. We have frequently urged earlier neurosurgical intervention, preferably before major signs have developed. However, this procedure is of such a drastic nature that one can easily understand how reluctant a neurosurgeon might be to undertake it with only minimal indications. The therapy of acute encephalopathy accordingly remains unsatisfactory and again we must urge that prevention rather than cure be our first line of defense.

In conclusion it should be stressed again that lead poisoning continues to be recognized with disturbing frequency in cities which are alert to the disease and equipped to provide analytical analyses for lead; that the source of the lead nowadays is paint which was applied some years ago and which has been allowed to fall into deteriorated states; that the illness primarily involves one to four year-olds, and strikes almost entirely in the summer months; and that the disorder is virtually confined to the socioeconomically deprived slum areas. It should further be stressed that specific therapy has not met with great success once intoxication, and especially encephalopathy, have occurred. EDTA therapy, although it accelerates the removal of lead manyfold, only removes a relatively small amount of lead compared to the total in the body. Accordingly, the major effort in childhood lead poisoning must continue to be to prevent exposure. The responsibility for this effort should rest primarily with our public health departments.

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DISCUSSION

DR. HARRIET L. HARDY: How is a diagnosis of childhood plumbism made at postmortem if the diagnosis is not suspected? I asked this out of interest in the problem of porphyrin metabolism. Dr. Maloof and I have often wondered if one demonstrated porphyrin in fresh postmortem tissue in the central nervous system, possibly explaining some of the symptomatology in adults such as lead colic.

I would like to ask Dr. Smith to push the idea that it is important to immediately remove as much lead from the soft tissue as possible. Isn't the problem rather to remove the lead from circulation? Isn't this the lead that is harmful?

Also, I wonder if he isn't too discouraged about not removing all of the lead. If one could stop the exposure, it seems to me that one need not get discouraged about a number of courses of calcium EDTA. We have thought that when the soft tissue lead is removed with this drug and the drug is stopped, the lead comes from the skeleton into the soft tissue, and this can be repeated over and over again with the judicious type of therapy that both Dr. Miller and Dr. Smith have been emphasizing.

I remember a case we had on the metabolic ward at Massachusetts General of an adult storage battery worker with acute lead poisoning, and we gave him EDTA every day consecutively for a whole month. He got to the point where he was excreting pretreatment levels of urine, but if we rested him from the drug for a day or two, then the lead excretion went back up again to the same level it was at when we began this therapy.

This suggests that one can keep pulling lead into the soft tissues. Surely this is all still somewhat mysterious; the body has stored the lead away

to prevent it from producing toxic effects. Yet the exacerbation of cerebral symptoms 24 to 48 hours after the beginning of EDTA that Dr. Smith has been telling us about, Dr. Byers tells me he has little evidence of on children. It is certainly not seen in adults to my knowledge. Apparently Dr. Miller hasn't seen it. Could the rate at which the drug is given be important?

Dr. Laslo, who has had a lot of experience with this drug in bringing down high blood calcium levels, has suggested this from his toxic effect experience that this has to do with the rate at which the drug is given, but perhaps the best thing to say is that it is a difference in vulnerability of the central nervous system of the child and adult.

I was very much interested in Dr. Smith's use of hypothermia. It seems to be a highly intelligent move. Does he keep on using the calcium EDTA at the same time in view of what he told us about the exacerbation of cerebral symptoms?

I think all three of us are agreed that oral EDTA is only to be mentioned to be condemned, and I won't go into the reasons for it. That has been well done.

Certainly the three of us agree that in situations of acute toxicity, EDTA is highly useful.

I think it is important to mention now that the rate of exposure must be crucial in deciding acute effects particularly in the adult. I think the childhood problem has been so well gone over by others I won't mention that, but my clinical experience suggests that the body has a fantastic ability to handle lead if it isn't presented with the lead too rapidly, and this rate at which the lead is presented to the body must have a lot to do with the differences in clinical course and experience that Dr. Belknap reported yesterday and in the few cases of Pb poisoning which I described briefly in earlier discussions. So there is no question but that we would all agree that judicious use of EDTA for acute cases is surely the best treatment.

Chronic toxicity by which I mean the result of exposure to low levels, above permissible level exposure of lead over a long period of time with laboratory evidence of lead effect plus illness, this situation in my opinion, Dr. Miller, calls for the judicious use of short, slowly given courses of CaNa EDTA. We have been very much impressed with the porphyrin and hemoglobin abnormalities returning to normal with such treatment. I feel no hesitation in the wisdom of suggesting this, the routine being done over and over again.

I would like to talk briefly of something we have been doing. That is to use a single dose of calcium EDTA intravenously diagnostically. I think this may have real merit.

We showed that three adult volunteers from our staff at the General Hospital excreted from an average of .05 mg of lead per liter up to .5 mg of lead per liter with a single dose of 2 gm of EDTA intravenously. This is a rough base to work from. If one gives a single dose to a man with a documented exposure to lead who is being a puzzle, as in Dr. Hine's case, and I have two or three similar cases, and one gets a tremendous really important increase in urinary lead excretion and this can be corroborated with one or more signs and symptoms of lead intoxication, then the diagnosis of harmful lead effect is made. This strikes me as being an appropriate diagnostic maneuver carrying very little, if any, risk.

Yesterday I was listening with interest to the repeated assertion that we no longer have epidemic groups of cases of industrial lead intoxication. There is no question about this, but we have still got a group of important cases that need to be studied. I think they are missed, and they are incorrectly diagnosed sometimes if lead is not a suspected etiology. They are often impossible to diagnose. There is a nonspecificity to many lead caused signs and symptoms.

Because of such nonspecific syndromes mimicking other diseases, I would suggest to this group that you consider the use of EDTA in single dose for diagnostic purposes.

I would like to close just by mentioning the fact that the complexing agents are certainly here to stay.

Kety and Letnoff, I think, get credit for suggesting this earliest. We have the reports of Shubert, Foreman, Laslo and others, and now that we are in this brave new world of ours, where there will be inhalation of heavy metals of toxic potential, this expansion of knowledge of chelating agents I think is very important. The list below shows a few new chelating agents which I culled out of the literature: Penicillamine — B, B - dimethylcysteine. Ca DTPA — Calcium salt of Diethylenetriaminepentacetic acid. CDTA — Cyclohexane 1, 2 - transdiaminetetraacetic acid.

Penicillamine has been tried in handling abnormal copper metabolism for Wilson's disease. Diethylminetriamine pentacetic acid. This surely suggests that the concept of complexing damaging metals has caught on and will be developed with safe, manageable compounds in the future to take care of the damaging effects of metals.

MR. P. F. MURPHY: I am not a physician, and I have been enlightened in the last two days and confused also. I would like to hear some other doctor's opinion on the use of EDTA in diagnosis that Dr. Hardy has brought out.

DR. R. F. BELL: It is possible that a provocative lead excretion study may be helpful in determining that a man has an excessive body burden of lead when the usual lead studies do not reveal this burden. Until early 1955 we in Colorado believed, as most others, that a man did not have lead poisoning unless he showed excessive amounts of lead in his excretions and blood. Early in 1955 Dr. Sherman Pinto referred an unusual case to us for diagnosis and care from a lead smelter plant located at 10,000 feet. This Spanish-American, 36-year-old male, had over 10 years of occupational lead exposure, and during the last eight years of that time he had had periodic urinary lead studies that varied in a normal range from 0.08 to 0.20 mg. per liter corrected. For ten days prior to our seeing him, his own physician had given him 15½ Grs. of sodium thiosulfate, intravenously, daily, with no

change in his presenting complaint of loss of a working use of his hands and numbness of his forearms and hands, of one month's duration. He denied and we were unable to obtain any past history suggestive of lead poisoning. Physical examination revealed dilatation of his left pupil, weakness of his left cheek, a minor lead line, gauntlet anesthesia to his elbows, loss of deep tendon reflexes in his forearms, weakness in his forearm supinators and pronators and an inability to extend his wrists and fingers. Laboratory examinations showed a normal spinal fluid and normal kidney and liver function. This man showed a moderate hypochronic anemia, with a hemoglobin of 11.75 Gms. The expected normal at 10,000 feet altitude is 17 Gms. There was no basophilic stippling nor reticulocytosis. His white count was 13,700 with a normal differential. The blood lead was 0.07 mg. per 100 Gms. and his 24 hour urinary lead excretions were 0.08 mg. per 24 hours, while his daily fecal lead excretions varied between 0.28 mg. and 0.40 mg. for 24 hours. Because of the typical neurological findings, anemia and history of lead exposure, we made a presumptive diagnosis of lead poisoning in spite of the relatively normal body burden of lead as reflected by his blood, urine and fecal lead contents.

After four daily intravenous treatments of 3 Gms. of Ca EDTA, there was some return of his forearm deep-tendon reflexes, he could extend his fingers and wrists better and his gauntlet paresthesia, inequality of pupils, facial paralysis and lead line had disappeared. During these four days of preliminary treatment he excreted 38.5 mg. of lead. After three months of intermittent treatment with a total of 60 Gms. of intravenous Ca EDTA and 42 Gms. of oral Ca EDTA, this man was clinically completely well and returned to his former work with no disability.

Since this case, several similar cases with normal range pre-treatment lead studies have come to our attention and have been treated with Ca EDTA with equally gratifying results. One case was successfully treated with Ca EDTA in 1957, where in 1951 with the same complaints, we had suggested, but had refused to make a diagnosis of lead poisoning because his qualitative body fluid lead studies were within what we, as well as others, then considered normal limits. In these cases with the dramatic remission of symptoms after Ca EDTA, the increase in their lead excretion was also dramatic. It occurred to us that in certain cases where relatively normal lead studies are found, with symptoms possibly compatible with lead intoxication, a provocative lead excretion study might be of value.

To do a 3 Gm. Ca EDTA intravenous provocative test and collect a 24 hour urine specimen is a little clumsy. When we studied the partitioned excretion of lead in a 24 hour period after using 3 Gms., 1 Gm., and 1/10 Gm. of Ca EDTA intravenously, we found that the cumulative per cent of 24-hour lead excretion after the end of the intravenous infusion of Ca EDTA between the limits of a 1/10 Gm. and 3 Gm. dose followed a very reduplicatable curve equal to 72.4 log t, when t is the time from the end of the intravenous infusion in hours. A preliminary study of the increased amount of lead excreted after a provocative test with 1/10 Gm., 1 Gm., and 3 Gms. was in the ratio as 1 is to 1.8 is to 3.3 times respectively. This means that 3.3 times as much lead will be excreted in the urine of any particular individual after 3 Gms. of Ca EDTA, as compared with amount excreted after 1/10 Gm. of Ca EDTA intravenously.

We studied individuals with lead symptoms and a history of exposure and compared their excretions with several normal subjects with no symptoms or history of lead exposure, before and after treatment with Ca EDTA. In the lead-exposed cases the ordinary 24 hour urinary excretions of lead often overlapped the normal studies, but a distinct separation of the exposed and non-exposed groups could be determined from the amount of increased 24 hour lead excretion after 3 Gms. of Ca EDTA. From these studies we have tentatively decided that if the increase in the 24 hour urinary excretion after 3 Gms. of Ca EDTA intravenously is more than 1.2 mg., then it is presumptive that the individual has more than a normal increase in his body burden of lead. If the increase is less than 0.62 mg., then he presumptively does not have an abnormal increase in lead body burden. Comparatively this means that after 1/10 Gm. of Ca EDTA, intravenously, which can easily be given from a syringe and rather rapidly, an increase of 0.36 mg. in 24 hour urinary lead excretion would be presumptively positive, and less than 0.20 mg. would be presumptively negative.

You can see that with the 24 hour cumulative percent curve, a provocative test can be easily performed in an office under controlled supervision. A man wastes his urine in a bottle and immediately is given 1/10 Gm. Ca EDTA in 10 cc. of water intravenously and the exact time noted. The patient then does not void again for three to six hours, and the three- to six-hour specimen is collected and the exact time is recorded under direct supervision. The amount of lead found in this specimen is then corrected to 24 hours on the cumulative per cent curve for his 24 hour excretion.

In conclusion we believe that a provocative excretion study is of value under certain circumstances, but that considerable study and corroboration is needed before it can be accepted as a criteria in lead surveys or diagnosis. One word of caution — we have found that if there has been recent treatment with Ca EDTA our provocative criteria fails. A four- to six-weeks treatment-free period should be allowed before evaluating a provocative study.

Before closing I would like to say a word in defense of the treatment of lead poisoning with Ca EDTA. We have been afforded the opportunity to supervise the treatment of nine cases of inorganic lead poisoning in adults with what we previously assumed were permanent neurological changes and have seen miraculous recoveries after treatment with Ca EDTA. One of these cases had forearm extensor weakness, wrist drop, and other neurological disturbances for 20 years while remaining out of exposure without improvement; and after

one and one-half years of intermittent Ca EDTA treatment he recovered normal function. This man was being retired as totally disabled, supposedly with CNS lues, at the time we first saw him, but was returned to normal work after his treatment with Ca EDTA. He had unrecognized complicated lead poisoning, not CNS syphilis.

We have seen severe colic relieved by Ca EDTA when calcium gluconate, morphine, Demerol and Dilaudid have given no relief of pain. We have seen a case of hypochromic anemia, fatigue, weakness, and vague joint pains from lead respond within days after Ca EDTA therapy, yet he had formerly failed to respond, after removal from exposure to lead for about a year, and treatment by several excellent internists with liver, B_{12} and iron. After a short period of daily intravenous treatment, this case was later given oral Ca EDTA by his physician and immediately developed a 1+ albuminuria which cleared after four months. His kidney function studies showed no abnormality. His own physician is certain that the temporary albuminuria was from oral Ca EDTA. Other than that one instance of temporary albuminuria that developed after oral Ca EDTA, we have not seen any adverse effect from two- to eight-week intermittent treatment with four or five daily intravenous 3 Gm. doses, nor from the sporadic experimental use of daily 3 Gms. oral Ca EDTA. We have given several hundred treatments with Ca EDTA since 1952. Some individuals in our group with neuropathies have been treated intermittently for as long as two years.

MR. CARL WALTERS: Could I ask you, were all these men hospitalized, or non-working?

DR. BELL: All the men with neuropathies, except one, were hospitalized during their original study and treatment. After partial recovery they were followed on the job and hospitalized only intermittently every month or six weeks for several days of treatment and study.

DR. H. N. SANFORD: We do have a serious problem of lead poisoning in children which is based on certain factors.

The first is the age of the child. They are usually from 18 to 36 months of age, because that is when they begin to walk around and pick up things. Secondly, they have to have a certain environment. This environment is a home where the inside paint and putty is over 50 years old, so that they can obtain the lead from the old paint that flakes off. And finally, this usually occurs in hot weather when dilated capillaries and a mild acidosis brings the absorbed lead back from the bones into the blood stream.

Here in Chicago, for example, we only observe the severe symptoms of lead poisoning from June to September. They occur in every hot spell. All of the children we see during the year with lead poisoning are during these months.

The next important point is that of diagnosis which is rather simple. As a history we have the factors I have mentioned. Clinically we have a child who is irritable, has anorexia, is losing or not gaining weight, has persistent constipation and periodic vomiting without any particular reason or discomfort.

We have the rule in our clinics that if such symptoms occur in a child of this age group in the summer time particularly, or even at any other time, these children must have their urines examined for coproporphyrins. I did not hear this mentioned, but we have found it to be a most reliable screening test and very simple to do. All you need is 5 mls of urine, 5 mls of ether, three drops of acetic acid, and shake well. This is examined under a Wood's light after 15 minutes. If the child has an excess of lead secretion, the urine will show a reddish color. The intensity of color is not consistent with the amount of lead excreted. If you get any reddish color change at all, the child has lead poisoning.

The next important thing is to initiate immediate treatment. Don't delay. Obviously the child should be removed from the source of lead, but this is of course not always possible. Next, active attempts should be made to get the lead out of the tissues. This can be done by a variety of methods. Twenty-five years ago we used to alkalyze the child; however, we found it was more dangerous to pull the lead out rapidly than it was to leave it in.

I agree with all the therapeutic measures mentioned, but I would like to emphasize that initially the edema is more important than the encephalitis. Last year I got to the point where I felt that a decompression should be done on all of these children as soon as they showed the slightest signs of encephalopathy. This year I have changed my mind somewhat because we have had good success with the immediate use of certain dehydrating agents such as injectable urea (.5 gm per cc). So far this year we have used this initially and have not found decompression necessary. The main point is to do one or the other at once and not wait for increased pressure and convulsions.

DR. BYERS: Lead poisoning in children still does occur in the winter. We had a child last January or so that died of lead encephalitis, following chicken pox, which of course, doesn't respond to any of the drug treatments. He started to vomit and became unconscious. This was erroneously ascribed to chicken pox encephalitis. Nobody looked for lead because it was January. It is important to remember it does happen.

We have the same seasonal peak in Boston, exacerbation in the summer months, but still there are cases at other times of the year. There must be other factors than heat or sunlight or vitamin D that precipitate lead poisoning in some children and in other periods.

We had a bad accident with oral Versene when it was first under investigation. Our practice was to take the children in, get 48 hour urine sample to substantiate the lead poisoning, clean out the GI tract and give them some oral Versene. By mistake one child got oral Versene on the first day in the hospital. The child fell unconscious. He had not been seriously ill before, but his lead excretion went to something like 15.5 mg in the next 24 hours. His spinal fluid, total protein, went up very

markedly from somewhere around eighty to somewhere around 400 mg %, and I am sure that he was badly injured by this experience. If you give oral Versene with lead in the GI tract, you not only absorb the Versene but also absorb a lot of lead along with it. The Versene-lead combination isn't a one-way street, and it is possible to break it down in the tissues, and give out lead.

Then the last point I would like to make is about porphyrin excretion. There is a little evidence that sunlight has something to do with increasing the porphyrin output in existing lead poisoning. De Melo, I think it is, has inoculated rabbits and other animals with lead and exposed them to ultraviolet light with other things remaining constant and gotten a great increase in the amount of porphyrin output in the urine of these animals, so that sunlight, as other people have suggested, not only has something to do with the absorption of lead, but also has some effect on the metabolism of lead after it is in the body.

DR. H. H. STEINBERG: Before we get too enthusiastic about EDTA, I should like to caution you against considering it as a panacea in the treatment of lead poisoning. I believe it may have a real place in the treatment of acute plumbism in children.

I should like to caution you against its use in adults since many cases definitely diagnosed as industrial lead poisoning get well without the use of EDTA, and almost without the use of any definitive treatment. As was so clearly shown by Kehoe so many years ago, by removing these people out of the lead environment and treating the colic or anemia, these people get better.

The use of EDTA will never eradicate lead poisoning. As a matter of fact, Dr. Johnstone a few years ago in St. Louis pointed out that one of the plants in Los Angeles had stacked their shelves with EDTA instead of inaugurating a control program for the reduction of atmospheric levels of lead in the environment to safe levels. I think the important problem is as Drs. Hardy and Reznikoff emphasized yesterday, the one of diagnosis.

We are not educating the house officers, residents and interns at the hospitals. We are not getting to the general practitioners. We are not getting to the industrial physician who, by virtue of his proximity geographically to a plant that has a potential lead hazard, is the one that is called upon to diagnose and treat cases.

I would suggest that organizations such as this one, universities, industrial medical groups or medical societies establish panels of qualified physicians in the occupational diseases, so that doctors or house officers can consult with these physicians for advice as to diagnosis and treatment.

Hope for Gout Sufferers

A "happy accident" of medical research has led to the discovery of a powerful new drug for the treatment of gout which is now undergoing clinical trial by scientists at the National Institute of Arthritis and Metabolic Diseases. The drug, zoxazolamine has been widely used for several years as a muscle relaxant, but its possibilities in the treatment of gout are the result of a chance observation made during studies of the drug's metabolic breakdown in the body, when researchers noted large amounts of uric acid crystals accumulating in the urine of patients receiving the drug as a muscle relaxant.

Preliminary tests in several patients indicated that zoxazolamine was significantly more potent than any uricosuric drug now in use, and further studies show that the drug is approximately six times more potent.

In addition to zoxazolamine another uricosuric drug, known as sulfinpyrazone, is being studied at the Institute. The action of these two drugs appears to be additive, so that when given together they produce greater uric acid excretion than either drug does alone. These developments promise relief to gout patients who have not been helped by older drugs.

Responses of Human Subjects To Lead Compounds

Progress Report on an Experimental Investigation of Factors Which Influence the Responses of Human Subjects to Finely Divided Lead Compounds in the Atmosphere

• ROBERT A. KEHOE, M.D.
Kettering Laboratory
University of Cincinnati School of Medicine
Cincinnati, Ohio

I have made use of an unsatisfactory title for my contribution to this program because I didn't know how to give a better one. Perhaps you may come to the conclusion that it would have been better had we gone on with the discussion of the subject that we were dealing with just prior to this time.

I want to explain my purpose, however, and call your attention to one or two things which I think are of fundamental importance. We shall understand the problem of lead poisoning better when we understand the metabolism of lead in the human organism and when we know more about the physiology of this material, of this mineral element.

It may be of some interest to recognize that we probably know more at the present time in the field of the mineral metabolism about lead than we do about any other element. I see a shaking of heads. This is only because there are some new elements which, because of their newness, have been looked at with considerable intensity, but with respect to the older elements, those that we have been concerned with for the long pull — those which because of our familiarity with them we tend to think of as being well understood — I think I can say with reasonable safety that we probably know more about this in relation to lead than we do in connection with any other metal.

In any case, I wish to recount to you, in a very short space of time, what we have been undertaking to do over a period that began in 1955 and is still continuing: to further elucidate the metabolism of lead in the human organisms. After this, if time permits, I shall wish to refer to some practical considerations that relate to diagnosis and to industrial hygiene.

Over this period of time in the Kettering Laboratory, we have been devoting ourselves to a basic study of this problem. It began with an attempt to elucidate the occurrence and the distribution of lead in nature and in biologic materials. This has not been by any means completed, but the essential contributions which we have made to this field were published in their initial form in 1933. Then a few years later we began to study the metabolism of lead in human subjects under conditions of both normal and abnormal intake following the oral administration of lead, undertaking to determine precisely what happened under the conditions of prolonged, continued administration at variable levels of dosage.

The results of these investigations have not all been published, but to the extent that they have been published, they appeared over a period of several years ending about seven or eight years ago. Then about eight years ago, we began to study the other important variant of this problem, from the point of view of industry, namely — what happens to lead which is in the respired air; how and to what extent it is respired and retained in the pulmonary apparatus, what happens to the rates of absorption, retention, excretion under these conditions.

This has not been finished. After some eight years of work in this field we have completed now six experiments on four subjects, two of which have been duplicated. We are able to report our progress, and my reason for reporting this verbally is that it is, I think, unsatisfactory

to publish this material in titles here and there, in bits and pieces. Such reporting fails to accomplish our purpose, in that, as we have seen here today in the questions that have been raised, the pertinent facts about which we are in doubt cannot be presented fully and systematically.

In short, serial brief publications fail to present the problem in all of its facets in such a way that one can grasp its full significance. Therefore, we have withheld publication, and this is the third verbal report that I have made to interested groups as to what we have learned up to the present time.

I would like to discuss the backgrounds of this work further, but I may say that its primary objective is to understand the problem and all of its ramifications as far as we can under the controlled conditions of laboratory observations on human subjects. If a more specific objective were in mind in the group of experiments that are under way at the present time, it is the idea of appraising the whole area of respiratory exposure to lead in terms of such things as the standards that we are concerned with in the field of occupation; the standards which relate to the exposure to lead on the part of the community in general, with respect to what is safe on the background of our knowledge of the normal metabolism of lead; of the unavoidable exposure to lead, plus what we have learned in addition from industrial experience.

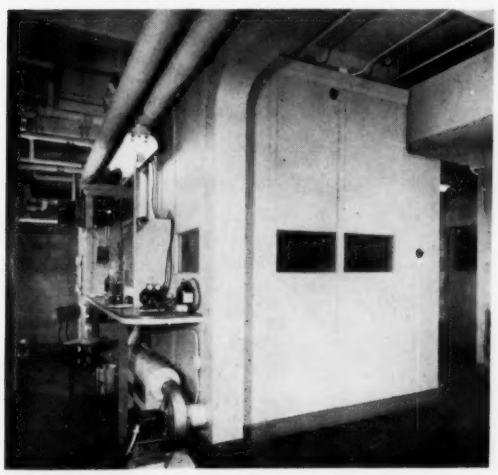
Beginning with Figure 1, we have a respiratory chamber, the outside of which is illustrated, this being essentially a chamber made by the use of standard metal partitions that are available at the present time on the market, plus the introduction into it of the necessary ventilatory and other equipment that would produce a dynamic experiment by which we can introduce into the atmosphere of the chamber a known concentration of a known compound of lead in a known state of subdivision, in which an experimental subject carries out his day's work on five days of each week for seven hours and a half a day. This procedure simulates the conditions of industry, but not those of community exposure to lead in the atmosphere.

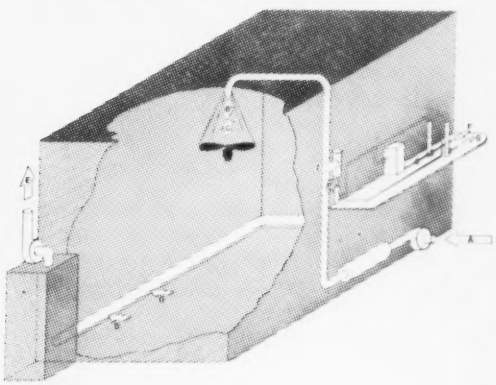
Figure 2 merely shows some of the details: the intake of air, the course of distribution of the stream into the chamber, the use of a fan below and at the end of the influent tube to dissipate the air throughout the room instead of using a mechanical distributor which would inevitably cause some of the lead to be deposited upon its leaves. The distribution system at the bottom is the means of removal. The material passes through an electrostatic precipitator to the outside where it goes into one of the main stacks of the laboratory, and the experiment is, therefore, contained within the unit area of the chamber itself.

The equipment located outside the chamber on a shelf is the means, in a specific experiment, of introducing the lead compound into the chamber at a known rate and concentration.

This room is equipped as an office. One cannot use an experimental subject in this kind of experiment without giving him something to do other than twiddling his thumbs for five days a week, seven and a half hours a day over a period of months, weeks or years.

The methodology from here on is that of having the individual who is the experimental subject collect precise duplicate samples of everything he eats and drinks in the course of a day, to collect all urine voided, to collect all feces passed in the course of this period of time and to maintain this regimen daily throughout the period of the observations, including a period of not less than six months preceding his introduction into the chamber, in order to establish the pattern and the character of his lead metabolism.





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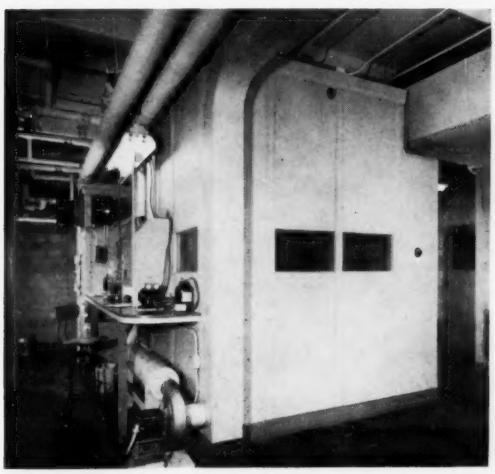

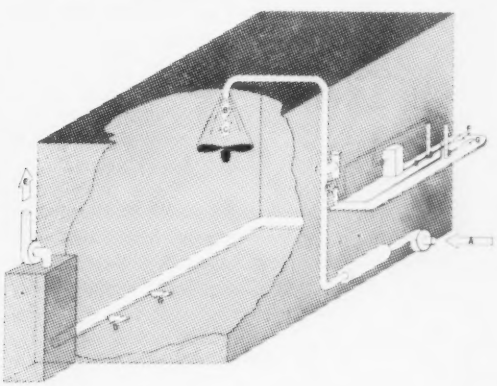

Figure 1 (Left)
Figure 2 (Above)

I might point out to you at this point that while it is necessary to establish the initial metabolic pattern of this individual, this procedure does something more. The pattern of the lead metabolism is so clearly established in terms of present day community life that we can very easily detect not only whether a subject is normal in his behavior, but also whether or not he is a reliable subject. If he deviates much from the normal pattern it requires investigation.

Figure 3 shows an x-ray diffraction pattern which in this instance demonstrates the nature of the compound used. Since our early and traditional experience in this area of lead in the atmosphere has related lead oxide, we have chosen, for historical reasons and also for the ease of doing it, to use lead sesquioxide which is produced by the combustion of a small quantity of tetraethyl lead in a stream of propane through a Bunsen burner. By this means, you can regulate the size of the particle and the concentration of material entering in terms of the speed at which the tetraethyl lead is fed to the propane stream.

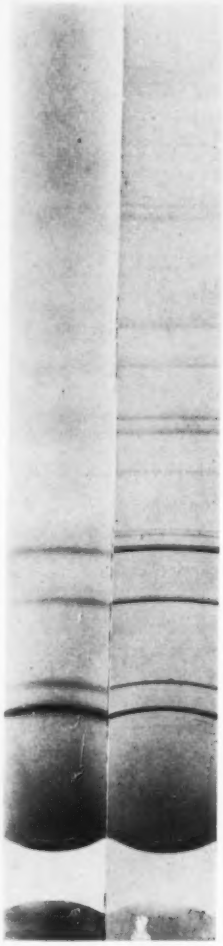

Figure 3

This provides a completely reproducible system for producing lead of a known size of particle, of a known chemical character, and at a known and very steady rate of production.

Figure 4 shows the electron microscopic picture of the lead compound used in the chamber, in this particular instance, in an experiment in which lead sesquioxide of the mean size is .05 micron. (Individual particles in small numbers are as large as .17 micron.)

Figure 5 shows the distribution of the particle sizes, and you may see that there is an even distribution of the particles in the chamber.

Figure 6 illustrates a troublesome procedure and one I may say that is still troublesome. This method shown is not entirely satisfactory. We

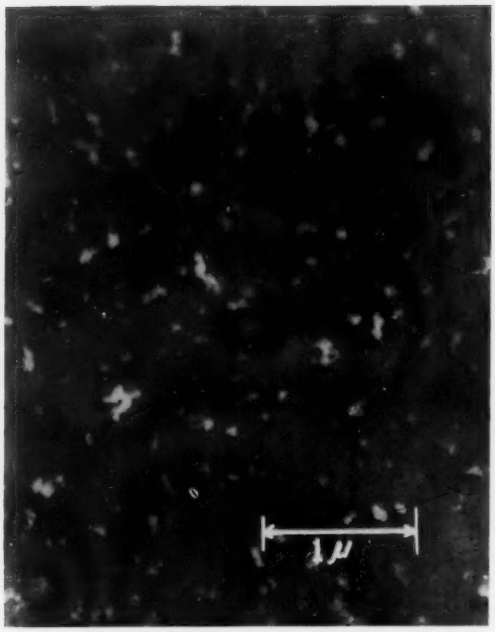

Figure 4

are put to the necessity, in determining how much lead this individual takes in and retains under these conditions, of being able to deter-

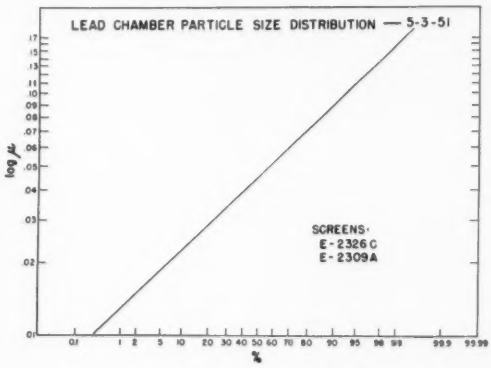

Figure 5

mine the lead in the expired air, and we have devised a simple method of doing this. It enables

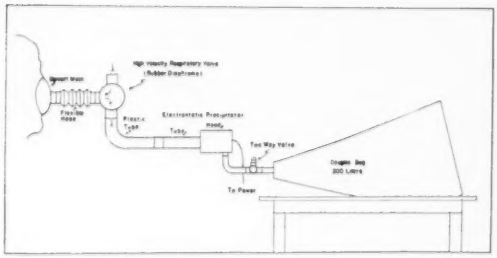

Figure 6

the individual, while breathing air contaminated with lead, to expire through an electrostatic precipitator into a Douglas bag. The expired air passes through the precipitator first at the shortest possible route, rather than through the Douglas bag. By this means we have been enabled to determine approximately, at least, the extent of the pulmonary retention of lead, and you will recognize that on the basis of the calculation of the lead concentration in the air and knowing the respiratory volume and rate, we are able to determine what portion of the lead breathed in in the course of this seven and a half hour period was actually retained and absorbed, and we are able to determine, as I will show you later, something of what its fate has been.

As I indicated, we have done six experiments, one of which continued for five years and two months. The second one continued for four years and four months; the third one for two years and six months; the fourth one for two years and seven months; the fifth, for two years; and the one which is at present in progress has now gone on for a year and a half and will not be completed for another two years.

These are troublesome experiments to carry out, costly in terms of the time and effort of all the people involved, and they can be justified only on the basis that the questions that have been raised here this morning and through yesterday about the oddities of the behavior of lead under a variety of conditions can be answered satisfactorily in no other way than by this method.

Since time will not permit me to go into the individual experiments, let me conclude with these few remarks.

1. There have emerged from these experiments thus far, in accordance with the variables of dosage and particle size, three major facts. One of them is the discovery of what happens when the respiratory exposure is discontinuous. The individual reaches a plateau, with respect to his rate of urinary excretion and the concentration of lead in his blood, when he is exposed for five days a week rather than seven. If we give lead by mouth every day, or seven days of each week, the concentration in the urine and the accumulation in the body goes up at a steady, essentially constant rate throughout the whole period of exposure, for as long as five years.

In these experiments the subject reaches a plateau in from six to eight months, at which time the height of the plateau is indicative of the severity of the conditions of the exposure.

2. The next point, and the only one which I wish to emphasize at this time, is the fact that when we change the size of particle two things result. The particles of small size (0.5 micron) are retained in the lung to the extent of about 35% to 40%. With a larger particle of about one micron we note a slightly greater pulmonary retention, around 40%, 45%, up to 50%. A very considerable proportion of the particles of 3 microns is strained out in the upper respiratory tract and appears in the feces. At this point the level of the fecal content is differentiated sharply from that due to the food and, at the same time, the total rate of lead absorption, in proportion to the lead content of the air, decreases.

I think you will understand why I said, at the start, that it would be difficult to present to you much in the way of an account of what has been done and learned by these experiments. I have believed it to be worthwhile, however, to bring you a progress report indicating that this work is continuing, and that we are carefully examining step-wise the factors that influence inhalation, as well as those which influence absorption and excretion under the conditions of inhalation.

DISCUSSION

DR. JOHN LAUER: From the charts that were put before us this morning a few questions arose in my mind. Following the period of the inhalation of lead sesquioxide, there was a rise in the blood level and concomitantly in the urinary excretion of lead. If I noted the charts correctly, the excretion dropped off in the urine rather abruptly, whereas the content of lead in the blood after discontinuation of exposure tapered off rather gradually. In Dr. Kehoe's early work in the Twenties or early Thirties lead was given by mouth. After the dosage period was over, the excretion tapered off over a rather long and gradual period.

This did not seem to be true in the subjects shown here this morning. I would ask for comment on that.

Another point that wasn't clear to me is the matter of some 30% or 40% of particles which were retained in the respiratory tract following additional exposure. I wonder if this was retained or deposited on the respiratory mucosa. If it was deposited, how much of it was lost in the mucous, and therefore swallowed later or expectorated?

These experiments are obviously not completed. The use of finely divided particles of different compounds was the program's statement and yet today Dr. Kehoe reported on only one, the sesquioxide of lead.

One other point that I would like to raise, and that is the matter of influencing excretion. It was stated that only EDTA, BAL and water influenced the curve of excretion. One wonders about this in respect to the day-to-day variations in the curve, whether there are other factors not yet known that may have an influence.

DR. D. P. LAUGENOUR: This work of Dr. Kehoe's ties in completely with what we must know about what

we are going to accomplish, or are accomplishing with the use of EDTA. There have been numerous case reports on cases that were treated by EDTA which indicated that at the end of a relatively short course of treatment, the urine and blood samples had returned to what we consider a normal level. Long continued exposure, as we have in many cases of lead poisoning in industry, as also indicated by Dr. Kehoe's work, shows that these cases, if left alone to the normal metabolic and excretion processes, would take approximately twice as long to return to the normal line as to get up to their high level.

Someone else commented to the effect that EDTA, in forming a chelate with lead, was not a one-way proposition; but followed the laws of chemical balance, in that there is always a reversible action and it simply goes in one direction to a point of chemical balance.

If this is so, then it would be possible, in giving EDTA in too large a dose, to increase the actual toxic amounts of ionizable lead present in a critical case of toxicity, such as in a child with encephalitis. In my experience with results and data in the use of EDTA, I have had no case that has returned to normal levels even after prolonged use of EDTA far past that required for the relief of symptoms. Although urine levels would return to non-exposure levels after six to 12 weeks' freedom from the use of the drug, they still come back to practically the pretreatment levels until after three to six months' intermittent use of EDTA. This is exactly what one would expect from Dr. Kehoe's presentation, unless the drug were continued over a period of time that would be roughly proportional to the time that this patient was absorbing his lead, acted upon by the factor of the increased excretion due to EDTA. In other words, if a single injection of EDTA caused a 30-fold, 24 hour excretion of lead, we would have to say that that represented 30 days instead of one day of getting rid of his lead; and, of course, as the EDTA is continued to be given, the amount of lead excreted falls until it reaches a level where the mobilizable lead outside of the bones is all excreted. But as soon as time allows, chemical equilibrium brings the blood back up to the balance determined by the total amount of lead in the system, which means in the bones. Therefore, to accomplish deleading, EDTA would have to be used over a period of time twice as long as the patient was accumulating his lead, divided by the multiple of the number of the rate of excretion caused by EDTA, and in most cases EDTA has not been used for that extended period.

DR. BELKNAP: Yesterday Dr. Reznikoff emphasized the importance of the clinician considering all the diagnostic possibilities in a lead exposure case, including nonlead conditions. I have two cases in point in the hospital right now. They were operated upon within the last week. They both presented themselves as "foot-drop," due to lead. They were fortunately not from our plant. In fact, we have never had a case of foot-drop in our own storage battery industry.

The places where we see most of the peripheral neuritis lead palsy cases, there are not very many of them, I have probably seen only six or eight, have been in the brass foundries where there is a long, continued low exposure, with low level of lead absorption.

One of these cases was a furnace charger in a smelter which was melting up old smashed battery plates. Though it was a relatively small operation, they usually were able to melt up two or three of these big semitrailer loads of smashed batteries.

They had only eight or 10 men exposed. This exposure was so intense at first, however, at one time I recommended that the plant be closed, pending adequate engineering ventilation. Thereafter, these cases were not sent to me.

They are still in operation, with only a fair amount of engineering control. One of the men I had first seen in 1951 or 1952. He was charging a smelter from a small scaffold with the fumes so intense that when I was up there standing next to him I couldn't see him because of the fumes that were blowing back out of the furnace. Inside of two or three minutes, I was tasting plenty of sweet lead. He still had been working there, and finally developed a foot-drop. He had drifted around from one hospital to another. They first thought he had congenital porphyria. When he was finally sent to me for evaluation, I believed that he had a mild foot-drop, most likely on the basis of the lead absorption. But there were certain aspects of the case that did not seem clear, and that didn't add up to show that lead was causing all his symptoms.

He was having increasing paresthesia, or numbness and crawling sensations of his lower legs, extending up toward the chest with a constriction distress from the epigastrum right through to his midback. None of that sounded like lead to me. However, we did treat him for the foot-drop with Versene intravenously. With the resultant increase in lead excretion, the foot-drop disappeared entirely. However, he still had these other symptoms of paresthesia, so that we had a myelogram done on him because I didn't want to turn him out. The lead-liability was over with the clearing of the foot-drop. A myelogram was then done and we found a space-occupying lesion from the fourth to the sixth dorsal vertebra. A neurosurgeon operated on him this week and found a localized arachnoiditis. The patient had treated lues in the past. This was so localized that it was beginning to pinch off the spinal cord itself.

That is one case where, if we had not pushed the diagnostic procedures more or less to the nth degree, probably somebody would have made a claim that this entire situation was due to his previous lead absorption. The operation showed really a localized spinal cord lesion unrelated to the occupation.

At the same time, I had in the hospital another man with a bilateral foot-drop. The attending neurologist felt it must be due to lead. This man was a hunter and told me at great length how he never even bothered to sift the lead shot out of the duck

that he killed and ate, but just swallowed it, lead-shot and all. He was also operating a small stone cutting operation, where he used a lead containing lubricant on his machines. Whether that had anything to do with it was questionable, but anyway he did have a borderline blood and urine lead, but no stippled cells and no lead line. He certainly had a foot-drop, but then he began to develop weakness in his hands, in the extensors.

I myself have never seen a quadriplegia due to lead, but he had been rapidly developing that in the last few weeks. We also did a myelogram on him. We found that he had cervical and lumbar discs. They went in on him yesterday and removed the lumbar disc. Later, the cervical disc will be removed with probable cure of the quadriplegia.

There was another case where there was lead in the background. If we had not followed it through, because it appeared atypical for lead, I am sure that the carriers in both cases would have been paying permanent total disability before long.

Yesterday Dr. Hardy spoke of plumbism as still being present in modern industry. I certainly would agree with that. It still seems to crop up in the most unexpected places, particularly in the small, unsupervised plants.

I would like to briefly quote two or three cases that have been in my experience in the last few years. One was a scrap paper dealer with only three men in the shop. It turned out that he was baling paper which contained lead arsenate from a nearby insecticide plant. When he jumped up and down in the press, he stirred up plenty of lead dust with resultant inhalation.

Soon this patient wandered into a hospital. Nobody knew what was the matter because he was so confused. However, when the technician in the hospital found 400 stippled cells per 50 fields, she told the residents they had better look at the patient's gums. They then found a lead line from ear to ear.

Another such case of unsuspected lead absorption was an eight-man brass foundry where the boss himself was the first man to get "lead poisoning." He had many stippled cells and a lead line. There were five cases of lead intoxication — lead colic type — in that eight-man brass foundry. They had just started to pour brass, though they had formerly poured aluminum. They knew nothing about the fact that there was lead in brass.

Another small shop of eight or 10 people were making an "oilfree" lubricant. You may not have heard of that. They bore holes in bronze bearings and fill the holes with so-called marvelous "oil-free lubricant" incorporated in a wax-stick. Investigation finally showed that the oil-free lubricant contained 90% lead oxide. I happened to see this case after the man died. Nobody had any idea, even the boss, that there was lead in that lubricant. The patient would put this on a lathe and smooth it down with a file, blowing the lead lubricant dust directly into his face. The man was scheduled to have an operation for brain tumor before a blood count revealed many stippled cells, and close study also showed a marked lead line of the gums. The man died a few hours after the operation and then the occupational exposure was suspected. Then I was asked to investigate.

Now all of those last three cases had lead lines and stippled cells. I think this underscores the importance of considering the commonest type of lead diagnosis, using the simple methods of study for lead line and stippled cells. Lead poisoning, much of it unsuspected, is certainly still with us.

To conclude this summary, I think that after a careful consideration of history, including a careful occupational history and plant tour by the doctor, together with physical examination looking particularly for a lead line and stippled cells, and even quantitative lead studies of blood and urine, I still would make an urgent plea not to throw any very useful diagnostic tool out of the window. I refer especially to the study of the stippled cells which has been used for many years, and is still used in most of Europe.

I know that such study has recently been called an antique method, but whatever method is used, whether you use stippled cells or quantitative lead in urine or blood, I think there are two important things to be considered: these studies should be done serially and frequently, and the physician himself should study the actual work exposure.

September, 1958

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SUMMARY AND DISCUSSION

DR. THOMAS L. SHIPMAN: There are few industries that are as ready and willing to air and discuss their problems as the lead industry. I am sure that every one of us feels that the Association is to be congratulated and thanked for providing this opportunity again to consider the problems of lead.

I have learned a lot in the last two days, and it is valuable knowledge. One thing that this session has emphasized wisely is that in this whole matter of industrial health we are dealing with two skills, medicine and engineering. I do not think that either one is more important than the other, but on the other hand, I would say this. The doctor by himself can do a pretty good job. The engineer by himself can do a pretty good job, but only by working together and appreciating each other's responsibility and point of view can they do the sort of rounded out job that the exigencies demand.

Now, to those of you with long memories, those words may have a familiar ring. They were spoken on this same occasion ten years ago by Dr. Lanza at the opening of his summary of the meeting. To the two skills, medicine and engineering, which Dr. Lanza mentioned, I think we must include a third. As was so obvious this morning, the field of research is a bona fides member of the team. Today, I feel we must recognize it as such, recognize it cheerfully and realize that research has much to offer, that bit by bit it is slowly unlocking the problems of the physiology of lead which have been puzzling men for over the past 2,000 years.

We started off yesterday morning with Dr. Belknap's paper, and immediately one quite important point emerged. This was a point which was brought out not only by Dr. Belknap, but by Mr. Pallies, Dr. Reznikoff and Dr. Kehoe, all of whom stress the danger of establishing a diagnosis of plumbism purely on the basis of laboratory tests. An individual with plumbism is a sick person. The diagnosis must be established by the acumen of the physician on the basis of history, physical examination and with the confirmation of laboratory tests of a wide variety.

Dr. Schrenk brought out some points worth remembering. In his paper he brought up the fact that the numbers used for maximum allowable concentrations of necessity must be used as guides, and they are a compromise representing the pooled knowledge of a group of experts. They represent a compromise in another way, too. I think all of us will agree that the only ideal dose of any toxic material is zero. Establishing a maximum allowable concentration, therefore, must be a compromise between zero and an obviously toxic dose. This is obviously true in the case of radiation, the field with which I am at the moment most familiar. We like to have zero doses to radiation as we would like to have zero doses to lead throughout industry. If the job is to get finished, we cannot attain to this ideal.

One point should be kept in mind also. Mention was made of the occasional lowering of maximum allowable concentrations or permissible doses. In some cases it is perfectly true that a lowering of a maximum allowable concentration represents new knowledge, that the material is in truth more toxic than it was thought to be. In some cases, however, a lowering of this sort may reflect only an improvement in our own technology and our ability to protect people and permit us to approach more closely the zero ideal that we should strive for.

It certainly is to be hoped now that the controversy of lead paint inside tanks has been ended. Certainly the discussions of Herb Elkins and Herb Stokinger on this subject were thoroughly convincing to me, and I certainly have no worries about drinking water that came out of a tank painted on the inside with lead paint.

I would like to mention one point that arose in my mind while listening to Dr. Byers. Our methods for analyzing blood, urine and air for lead are constantly improving although they still leave something to be desired. One thing which we have not yet been able to do is to study not the amount of lead which is being excreted, not the amount of lead which is circulated in the blood, but the amount of lead which is fixed in bone where we can't get at it; it seems to me that it is equally important to know what is left behind as it is to know what has been excreted.

We really don't know accurately what the body burden, the total burden of lead in a case of plumbism at any degree you choose to mention, is.

Dr. Foreman pointed out a phrase in a paper by Leckie and Tompsett from the *Quarterly Journal of Medicine*, January 1958, which I would like to read: "In any group of people exposed to the hazards of lead absorption a limited number of cases of frank poisoning will result. In the remainder, however, signs of toxicity will not appear, the skeleton having successfully immobilized the major part of the absorbed lead.

"There is good evidence to suggest that many forms of acute stress" — and here he refers to work of Aub, Fairhall, Minot, Reznikoff, Brown — "that many forms of acute stress can bring about release of this skeletal lead and give rise to symptoms of lead poisoning."

I think this is something which we should keep in mind. In the case which Dr. Hine quoted yesterday and which has been referred to by Harriet Hardy and others, the release and the reappearance of circulating lead is a matter of interest.

This meeting, of course, would not have been complete without John Foulger. The statements which he made, I think, are incontestable. He is opposed to sin and in favor of virtue, but he has given us some very good definitions of what sin and virtue are. I will just point out one thing that he said: that a compliance with statutes does not provide immunity, that good faith is required. That, I hope, will be remembered.

As for Ted Waters' paper, he dwelled on worries that have bothered him. I don't think there is any-

one who is better qualified to consider the legal problems having to do with industrial medicine than Ted, and certainly if we lump together the statements made by John Foulger, Ted Waters and Arthur Johnson, we have some things to remember.

In Arthur Johnson's paper, I particularly remember his statement about the three criteria for acceptance of liability in compensation cases. First, the establishment of a true and positive diagnosis. Second, the establishment of an actual causative factor for the disease in question, and finally, the existence of true disability. I only wish that all of the members of all industrial accident boards understood this as well as Mr. Johnson.

Ten years ago there were two areas which really presented something new, something which probably would not have been considered had there been a meeting before that, in 1938. One of these was the study of solubility and particle size, an area which was not strictly new to some investigators, but I think it was rather new to much of the group at that meeting. The second new topic was the use of BAL in the treatment of plumbism.

This year we have two things that are new. We have Anna Baetjer's work on the effect of temperature, humidity and seasons, and the two papers on the use of EDTA in treatment, and Anna Baetjer's paper, in my opinion, was outstanding.

EDTA was not mentioned ten years ago. It didn't exist. BAL was the new thing, but in his paper on BAL, Dr. Eagle said: "I wish to suggest that although BAL has proved so effective in the treatment of certain types of heavy metal poisoning, there is no reason to believe that other compounds may not be developed which are even more effective and which, acting on the same principle as BAL, may serve to abstract lead from its combination with tissues."

I feel very certain that at the next session of this meeting ten years from now EDTA will have passed into limbo, that we will have new compounds which will do the job very much better than BAL.

We wound up with Bob Kehoe's paper, which was impressive. I wish to point out that what they are doing at Kettering is research in the grand manner. This is using man — getting him into what most nearly approximates a toxic working environment and studying him. It is a tremendous chore and I believe that Bob and his associates at Kettering are to be not only congratulated but encouraged to keep it up.

I would like to summarize and perhaps anticipate the 1968 meeting. There are certainly areas of ignorance in the field of lead toxicology, and it seems to me that the works which we will be hearing about 10 years from now will involve a continuation of the general studies on lead physiology and lead toxicology, studies such as those described by Anna Baetjer and Bob Kehoe today. We certainly would hope that 10 years from now we will have more precise laboratory tests for exact determination of the degree of lead poisoning, and certainly we have reason to hope that, 10 years from now, we will know more about the biological effects of small doses of lead. The fact that exposures and blood and urine levels are kept below a certain point, does not guarantee that damage isn't being done, damage which we are still unable to determine.

Now this is not anything directed only at lead. The same thing is true in a wide variety of fields. The ideal exposure is zero. Somewhere between zero and what we might call permissible levels there is an area which requires study, and I would hope that this will be a topic on the agenda of our meeting in 1968.

Cancer in the City

The incidence of a number of specific forms of cancer may be associated with socioeconomic status according to data from 10 metropolitan areas studied by the National Cancer Institute of the U. S. Public Health Service.

The most consistent relationship observed is a relatively high incidence rate for cancer of the upper alimentary tract, pancreas, respiratory system, and uterine cervix among the lowest one-third income group in each community studied. Further evaluation of such relationships will be needed to try to discover specific etiologic factors responsible for variations in cancer incidence in different population groups.

The study represents a statistical analysis of thousands of cancer cases examined in 10 large population centers which were surveyed in 1937-39 and resurveyed 10 years later.

The findings of this study are reported in a monograph, "Morbidity from Cancer in the United States," by Harold F. Dorn, M.D., and Sidney J. Cutler, which is available from the Superintendent of Documents, Government Printing Office, Washington 25, D.C.

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March, 1959

VOLUME XXVIII

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Baltimore's Lead Paint Labeling Ordinance

In Baltimore since 1931 there have been 631 cases of lead paint poisonings in children with 115 deaths. The majority of these cases resulted from the ingestion of dried paint on household interiors, including window sills.

That distressing situation has led to a Baltimore ordinance that took effect in July of 1958 requiring the labeling of all paint containers in which the contents include more than 1% of any lead component. Provisions are made for enforcement of this ordinance and for punishment of those found to be guilty of violation.

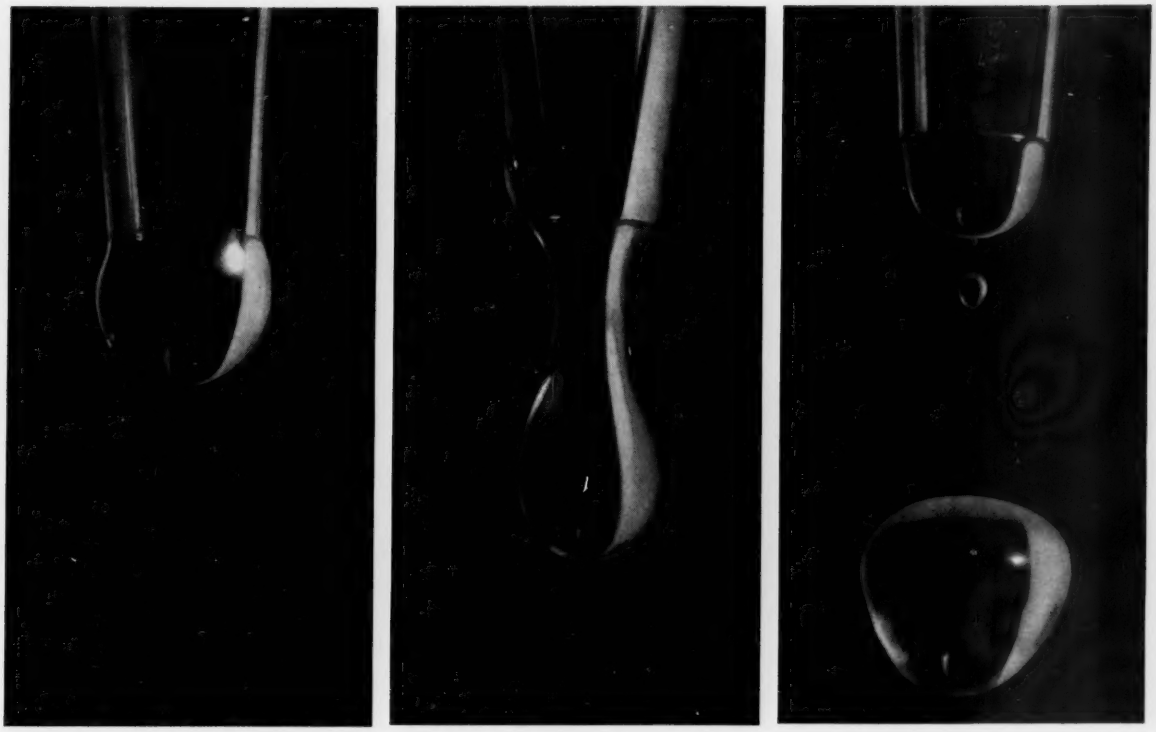
To no degree is this ordinance directed toward industrial lead exposures. Notwithstanding, many industrial workers will benefit by this form of protection. Many lead-containing paint coatings the country over bear no label disclosing lead content.

Lead is only one of numerous toxic agents that enter into industrially used materials bearing no label indicating harmful contents and no warning label of any character. By no means is this limited to paints or other coatings. Scores of other agents such as carbon tetrachloride or mixtures containing carbon tetrachloride are vended under trade names, in no way calling attention to potentially dangerous substances.

While the Baltimore ordinance may be salutory, industry's need is for far broader protective measures, in part to be achieved through listing of all major constituents on all labels. Not always is it necessary that warnings be included on the label.

Industrial physicians everywhere are sorely hampered in the process of investigating suspected chemical intoxication by the utter lack of information on the nature of the chemical substances to which exposure has been provided.

At the present time it is known that more than one major group is active toward the procurement of this form of protection. The lack of rapid progress in part springs from the fact that some of these organizations are at loggerheads with others, each insisting upon special rights or prior rights in this pursuit. In the meanwhile the damage goes on, and the diagnostic difficulties of industrial physicians persist.



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For these reasons ZANCHOL has shown itself to be a highly valuable agent in chronic cholecystitis, cholangitis and care of patients following cholecystectomy.

Administration: One tablet three or four times a day. Zanchol is supplied in tablets of 250 mg. each. G. D. Searle & Co., Chicago 80, Illinois. Research in the Service of Medicine.

SEARLE

Superior to aspirin in reducing fever in the "COMMON COLD"

In the management of symptoms of the common cold . . . fever, headache, malaise, muscular pains . . . why not weigh the advantages of Anacin over aspirin? Clinical literature has verified that a *combination* of analgesics in small doses appears to be more effective in relieving pain than either drug alone in its full analgetic dose.[1,2,3] Anacin is such a combination. Further investigation has demonstrated that one of the ingredients in Anacin (acetophenetidin) is superior to aspirin in reducing fever . . . aspirin having only 60% of the antipyretic action of acetophenetidin.[4] Well tolerated. No gastric upset.

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References: 1. Goodman, Louis S. and Gilman, Alfred: *The Pharmacological Basis of Therapeutics*, sec. ed., 1955. 2. Krantz and Carr: *Pharmacologic Principles of Medical Practice*, 1954. 3. Hammes, E. M. Jr.: *Pain Relieving Drugs*, J. Lancet 79:67, Feb., 1952. 4. Brownlee, George: *A Comparison of the Antipyretic Activity and Toxicity of Phenacetin and Aspirin*, Quarterly J. of Pharmacy and Pharmacology 10:609-620, 1937.

COMMENT AND OPINION

Ulcer Line

Realities of life in the Department of Defense finally have begun to receive attention at the practical level. Pentagon cafeterias now have two lines — one for regular food for those who haven't yet caught the occupational disease there; the other serving bland diet food for ulcer patients.

—*Des Moines* (Iowa) *Tribune*, January 8, 1959.

Rising Pressures

A study involving more than 700 men who have been working for a Chicago utility for as long as 40 years questions an old medical dictum that blood pressure inevitably rises with age.

It was found that 31% of the group had no increase. Their blood pressure in middle age is about the same as it was when they were examined at age 20 to 30. Jeremiah Stamler, M.D., who headed the study, also found that the steady-pressure group developed less than half as much heart or kidney disease as those whose blood pressure had risen.

The study was carried out in what was called an "ideal epidemiological setup." The subjects each had a thorough examination when they joined the company at an average age of 24 and have had regular examinations since. Records go back for at least four decades.

Dr. Stamler also sought to find whether the diastolic reading on blood pressure taken the first time had any predictive value as to whether a person would have some form of heart disease in middle age.

"There was a direct correlation between an elevated diastolic pressure in the 20's and heart disease in the 50's. It took the form of heart enlargement, angina pain, coronary heart disease, hypertensive heart disease or congestive heart failure. We found that an individual with a diastolic pressure of over 90 in his earlier years is a five-times greater risk for incurring heart disease than an individual with a lower reading."

Dr. Stamler believes the time is here when a physician can predict with a fair degree of reliability which persons are likely to develop early heart disease. The factors that seem to play a role are high blood pressure, overweight, high blood serum cholesterol level, faulty diet, heavy smoking, low thyroid activity, kidney disease, diabetes and familial tendency. Stress and strain and lack of exercise may be involved to an undetermined extent.

"Almost all of these factors are within human control and can be altered in the hope of lowering the risk," Dr. Stamler declared.

—*Chicago* (Ill.) *Daily News*, December 30, 1958.

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Stronger, more pliable, easier to handle.

Safer, quicker, easier
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Compulsory Retirement

A recently issued University of California study of 846 industrial workers in San Francisco and Los Angeles areas indicates that older male workers in firms with formal retirement policies tend to be less productive than older workers in companies without such policies. While stressing that this finding needs further substantiation through other studies, authors G. Hamilton Crook and Martin Heinstein comment: "We may speculate that these older workers, whose future was less structured, who had no expectation of a pension, and did not expect to be automatically retired when they reached a given age, were more highly motivated. They may have felt a continuing pressure to perform well on the job. Those workers who expected to retire on a pension at a given age were less motivated to continue to prove themselves . . . Should the hypothesis be substantiated, it would constitute a telling point against current policies providing for a compulsory retirement age."

An older worker's self-perception about his age is related to his work performance. Those older men who rated themselves as relatively young tended to do better on their jobs than those who rated themselves as older. Older workers who expected improvement in their status in next few years tended to have lower productivity ratings than workers who expected no change or a worsening of their positions. "It does not seem likely that pessimism as such would be conducive to superior work performance," the authors suggest. "It is plausible, however, that recognition of an insecure future might motivate some older men to work harder in an effort to improve, or, perhaps, merely to maintain, their position."

The attitudes of older workers toward retirement are generally negative, study reports. "The closer workers approach to retirement the less favorably disposed they feel toward it and the less they even want to think about it. In short, it may well be that in many older workers the whole idea is repressed." Among findings that back up this contention: Only 25% of men 50 years of age or older said they expected to quit work ultimately because they "will want to retire, be able to retire," compared with 42% of younger men. While 43% of older men expected to continue working as long as they were physically capable of doing so, only 31% of younger men said they'd continue working as long as they were able. About same proportion of older male workers (63%) as younger male workers (59%) reported they have no retirement plans. "One might reasonably have expected people who were within a few years of retirement to have formulated more definite plans about it than people who were 20 years younger," says study.

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Older workers were less receptive than younger workers to idea of a compulsory retirement age. Moreover, when asked at what age they thought workers should be retired, they tended to select older ages than did younger workers. "And yet, despite their predominantly negative attitudes toward retirement, more than half of the older workers did not think the worker himself should have a voice in determining retirement policy," study reveals.

An end of compulsory retirement policies was urged by president of American Medical Association before recent annual meeting of National Gerontological Society in Philadelphia. "We have seen a growing tendency to create employment policies calling for arbitrary retirement at 65 or 70," AMA president GUNNAR GUNDERSON, M.D. told meeting. These policies stem, in part, from belief of nation's young people "that retirement from productive work at 65 or earlier is a desirable goal," he said. "Their ideas about retirement are pretty vague — centered around fishing or similar pursuits, which now provide them with diversions from their work-a-day lives."

However, when individual actually reaches retirement, the life of case has lost its attraction. Instead, he discovers that productive work is the heart of life, DR. GUNDERSON observed. In urging industry to abandon compulsory retirement policies, the AMA president emphasized that repeated studies have shown that the healthy older worker is usually as good as his younger colleague.

—From *Industrial Relations News*, November 22, 1958.

Hearing Loss Committee

In accordance with the provisions of the Occupational Loss of Hearing Law enacted during the 1958 Legislative Session, Miss Angela R. Parisi, Chairman of the New York Workmen's Compensation Board, announced the appointment of a Committee of Expert Consultants on Industrial Noise and Occupational Loss of Hearing.

The Committee, composed of experts familiar with the various aspects of the problem of industrial noise and occupational loss of hearing, will present recommendations as to the most reliable and acceptable damage risk criteria and standards for the measurement and determination of occupational loss of hearing.

"Espresso" Coffee Wrist

Lipmann Kessel, an English orthopedic surgeon, describes a new but minor occupational disease among Italian instant coffee makers. He might have added that the French equally may be involved. To the uninitiated the apparatus employed is as complicated as a Chinese block assembly puzzle. Even the knowing ones must go through a series of deft wrist motions. Since every cup of coffee is made individually, the professionals of the restaurants must perform these motions scores of times daily. There is a toll—synovitis of the wrist, "coffee wrist." A cure may be found in Cortisone, but why have the disease in the first place? A stiffened wrist and a substitution of finger motions—and presto espresso, no synovitis.

BEADY-EYED HUMMINGBIRD, BALD-HEADED WOODPECKER, TOASTED ENGLISH SPARROW, AND THERE'S A COMMON WREN!
AGNES, YOU HAVE THE EYE OF AN EAGLE!
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SORRY GLADYS, I CAN'T. YOU KNOW HOW I AM THIS TIME OF THE MONTH.
I'LL BE RIGHT OVER.
HI, AGNES. WANT TO GO BIRDWATCHING THIS AFTERNOON?

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High Cost

Unrestrained by any general safety program capable of coping with them, industrial and occupational diseases are costing the general public in Texas at least $326,351,484 a year.

That is the estimate of the Industrial and Occupational Safety Study Commission created by the last Legislature.

The commission estimates that industrial accidents and diseases are costing employees $226,728,000 a year, making the total cost of occupational injuries and diseases at least $553,079,484 annually. This is about half as much as the total cost of the Texas state government annually.

—Felton West in *Houston* (Tex.) *Post*, November 11, 1958.

Healthy Attitude

Employee health, off the job as well as on, is becoming increasingly important to American business and industry. Nearly 90% of the managers questioned by the University of Michigan's Survey Research Center say they feel some responsibility for workers' health. The majority of the more than 250 respondents cited these reasons: Better health leads to greater efficiency; managers should feel a sense of obligation toward their subordinates. The survey was conducted for the U.S. Public Health Service.

—From *Supervisory Management*, July, 1958.

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new for total management of itching,[1,2] inflamed,[3,4] infected[5,6] skin lesions

Dermatitis repens
7 weeks duration

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Mycolog ointment

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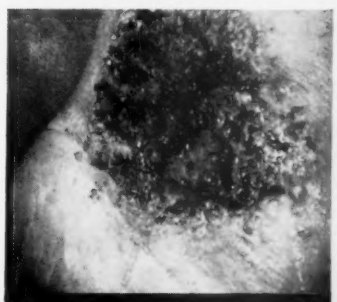

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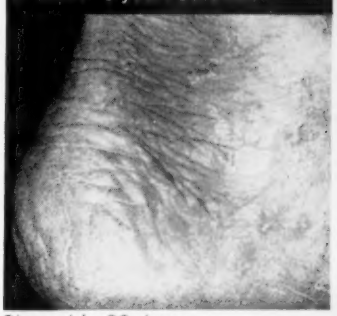

Cleared in 20 days

Mycolog Ointment – containing the new superior topical corticoid Kenalog – reduces inflammation,[3,4] relieves itching,[1,2] and combats or prevents bacterial, monilial and mixed infections.[5-7] It is extremely well tolerated, and assures a rapid, decisive clinical response for most infected dermatoses.

> "Thirty-one of 38 patients . . . obtained excellent or good control of dermatological lesions . . . [Mycolog] was highly effective, particularly in the management of mixed infections. Several recalcitrant eruptions which had not responded to previous therapy were remarkably responsive to the daily application of this preparation over periods of 2 to 3 weeks."[5]

For total management of itching, inflamed, infected skin lesions, Mycolog contains triamcinolone acetonide, an outstanding new topical corticoid for prompt, effective relief of itching, burning and inflammation[1-4] – neomycin and gramicidin for powerful antibacterial action[7] – and nystatin for treating or preventing Candida (Monilia) albicans infections.[8,9]

Application: Apply 2 to 3 times daily. Supply: 5 Gm. and 15 Gm. tubes. Each gram supplies 1.0 mg. (0.1%) triamcinolone acetonide, 2.5 mg. neomycin base, 0.25 mg. gramicidin, and 100,000 units nystatin in PLASTIBASE.

References: 1. Sheimire, J.B., Jr.: Monographs on Therapy 3:164 (Nov.) 1958. • 2. Nix, T.E., Jr., and Derbes, V.J.: Monographs on Therapy 3:123 (Nov.) 1958. • 3. Robinson, R.C.V.: Bull. School of Med., U. Maryland 43:54 (July) 1958. • 4. Sternberg, T.H., Newcomer, V.D., and Reisner, R.M.: Monographs on Therapy 3:115 (Nov.) 1958. • 5. Clark, R.F., and Hallett, J.J.: Monographs on Therapy, 3:153 (Nov.) 1958. • 6. Smith J.G., Jr.; Zawisza, R.J., and Blank, H.: Monographs on Therapy, 3:111 (Nov.) 1958. • 7. Monographs on Therapy, 3:137 (Nov.) 1958. • 8. Howell, C.M., Jr.: North Carolina M.J. 19:449 (Oct.) 1958. • 9. Bereston, E.S.: South. M.J. 50:547 (April) 1957.

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†Lhotka, F. M.: Illinois M. J. 112:259 (Dec.) 1957. Fabricant, N. D.: E. E. N. T. Monthly 37:460 (July) 1958. Farmer, D. F.: Clin. Med. 5:1183 (Sept.) 1958.

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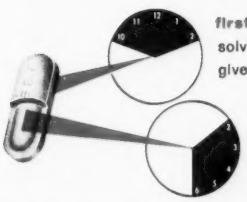

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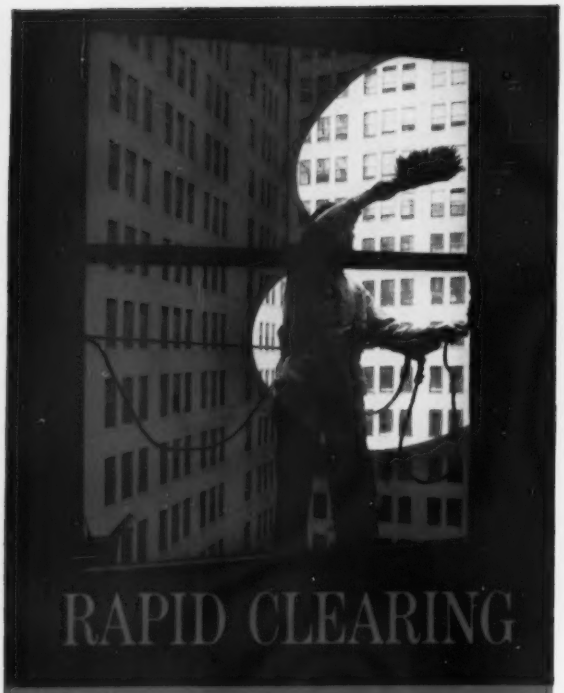

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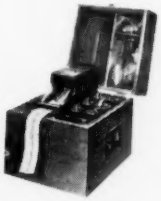

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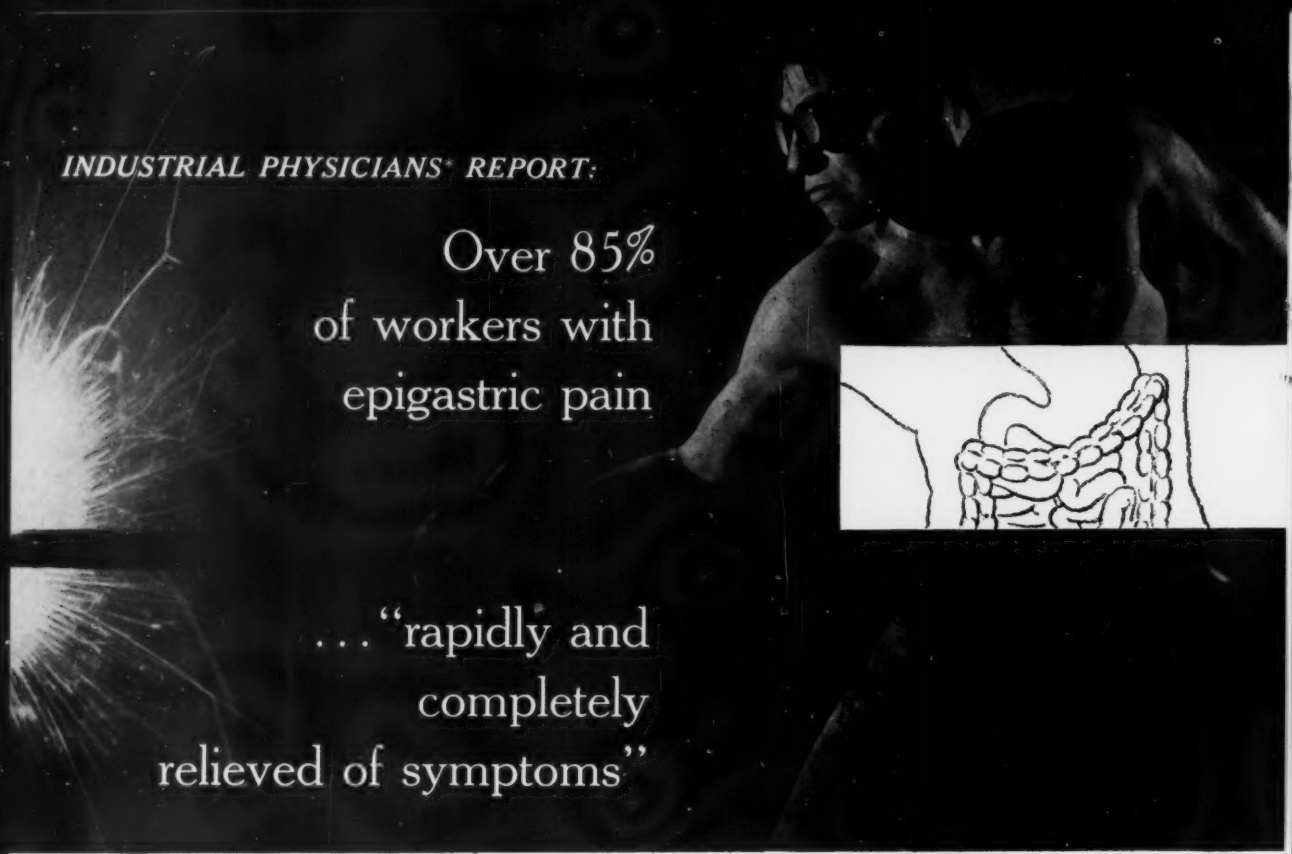

Noting that gastrointestinal symptoms were the chief complaints of more than half the workers reporting for treatment to their industrial clinic, Barden and co-workers* undertook an evaluation of Donnatal in providing rapid relief and minimizing absenteeism.

Based upon repeated clinical observation, case records, and progress reports over an eight-month period, the investigators conclude that Donnatal is "particularly effective for the relief of pain associated with smooth muscle spasm of the gastrointestinal tract." They observe also that:

"More than 85% of patients with epigastric pain and discomfort were rapidly and completely relieved of symptoms."

"... many employees were able to resume work within an hour."

"There was no evidence of undesirable side reactions."

DONNATAL® EXTENTABS** Robins

are particularly useful for industrial therapy, because once-a-day dosage provides effective spasmolysis for a twelve-hour period without the inconvenience of the customary four-hour dosage schedule. True *extended action* spasmolytic effects are provided by the special construction of Extentabs. Immediately after administration the equivalent of one Donnatal tablet is released, followed by the gradual and uniform release of the equivalent of two more Donnatal tablets, to provide sustained effects for 10 to 12 hours.

Each Donnatal tablet or capsule or each 5 cc. teaspoonful of Donnatal Elixir contains: hyoscyamine sulfate 0.1037 mg., atropine sulfate 0.0194 mg., hyoscine hydrobromide 0.0065 mg., phenobarbital (¼ gr.) 16.2 mg.—bottles of 100, 500, and 1000 tablets or capsules, and bottles of 1 pint and 1 gallon of elixir.

Donnatal No. 2 Tablets contain the same amounts of belladonna alkaloids with 32.4 mg. (½ gr.) phenobarbital per tablet—bottles of 100 and 500 tablets.

Donnatal Extentabs contain active ingredients equivalent to three regular Donnatal tablets—bottles of 100 and 500.

*Frank W. Barden, M.D., Paul S. Hill, M.D., William F. Mahoney, M.D., and Kenneth J. Cuneo, M.D., in a report from the Medical Department of the Saco-Lowell Shops and the Webber Memorial Hospital, Biddeford, Maine; published in the January, 1954 issue of the Journal of the Maine Medical Association (Vol. XXXXV, No. 1, Page 11).

**Trade Mark

DONNATAL® Robins

TABLETS • CAPSULES • ELIXIR • EXTENTABS**

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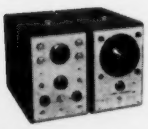
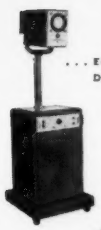
. . . TRUE ECG PORTABILITY



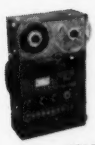
. . . VECTORCARDIOGRAPHY

. . . PHONOCARDIOGRAM
ECG RECORDING



. . . ECG MONITORING
DURING SURGERY

. . . MULTI-
CHANNEL
RESEARCH
RECORDING



. . . HEART SOUND
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You take it for granted that today's medical instrumentation is basically accurate and reliable. But *beyond* these expected fundamentals, the dependability—usefulness—and convenience of any instrument depends almost wholly on how much the instrument manufacturer *knows of your needs* and how well he has *applied this knowledge.* For more than 40 years, Sanborn Company has asked the general practitioner and medical school teacher . . . the cardiologist and researcher . . . the industrial physician and clinician, what *they* particularly need for *greatest* usefulness and value in diagnostic and research instrumentation. The instruments shown here are typical Sanborn answers to these needs . . . exemplified in the field of cardiography by the Model 300 Visette—the first ECG to make "18-pound portability" a practical reality. Since its introduction less than two years ago, the Visette has literally become the "travelling diagnostic companion" of over 4000 of your colleagues.

When you choose any instrument to provide you with information for diagnosis and research, consider the instrument's background and past—as a good gauge of its *future* value to you. Sanborn Company, Medical Division, 175 Wyman Street, Waltham 54, Massachusetts.

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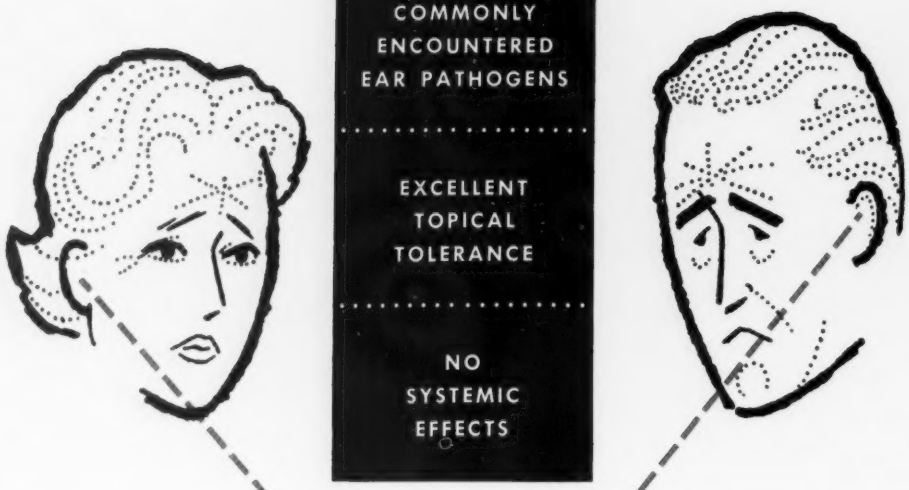

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OTOMYCOSIS
OTITIS MEDIA

Otamylon® and Otamylon® with Hydrocortisone

EAR DROPS

BACTERICIDAL
FUNGICIDAL
ANALGESIC
HYGROSCOPIC

Manner of Use:

After gently cleansing and drying the ear canal, Otamylon (2 or 3 drops or moistened wick) is applied three or four times daily.

Supplied:

Otamylon—bottles (15 cc.) with dropper. Otamylon c Hydrocortisone–15 cc. combination package to be mixed prior to dispensing.

Otamylon is a clear, odorless, sterile, viscid liquid containing:

Sulfamylon® HCl 5%
Benzocaine 5%
Anhydrous glycol q.s. 100

Otamylon with Hydrocortisone:
Same formula with 0.02% hydrocortisone.

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IMMEDIATE PAIN RELIEF

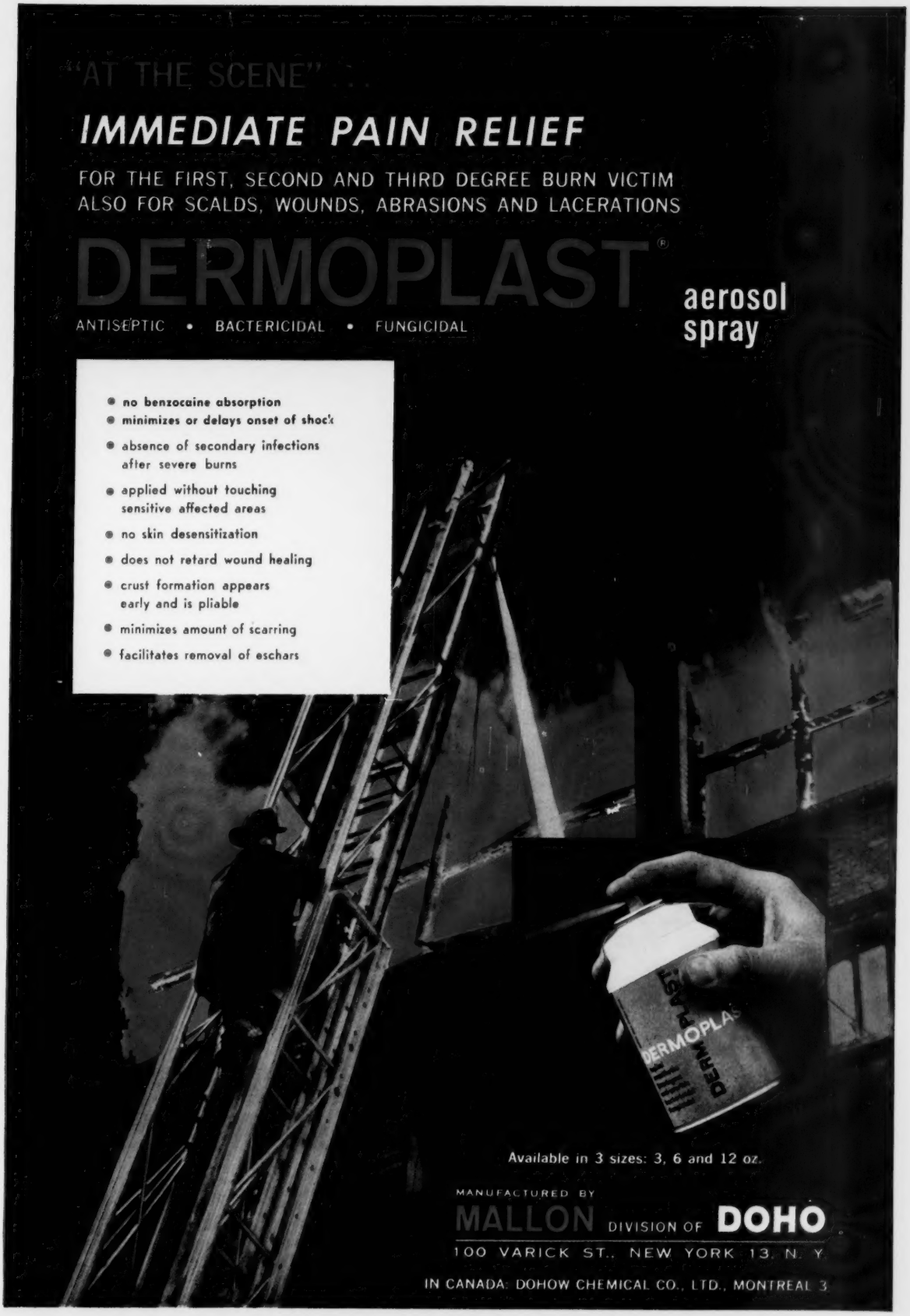
FOR THE FIRST, SECOND AND THIRD DEGREE BURN VICTIM
ALSO FOR SCALDS, WOUNDS, ABRASIONS AND LACERATIONS

DERMOPLAST®

aerosol spray

ANTISEPTIC • BACTERICIDAL • FUNGICIDAL

- **no benzocaine absorption**
- **minimizes or delays onset of shock**
- absence of secondary infections after severe burns
- applied without touching sensitive affected areas
- no skin desensitization
- does not retard wound healing
- crust formation appears early and is pliable
- minimizes amount of scarring
- facilitates removal of eschars



Available in 3 sizes: 3, 6 and 12 oz.

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running noses and open stuffed noses orally

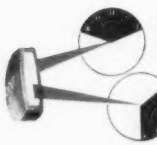
with TRIAMINIC, the oral nasal decongestant

- in nasal and paranasal congestion
- in sinusitis
- in postnasal drip
- in allergic reactions of the upper respiratory tract

safer and more effective than topical medication

- reaches *all* respiratory membranes systemically
- avoids "nose drop addiction"
- presents no problem of rebound congestion
- provides longer-lasting relief

Relief with Triaminic is prompt and prolonged because of this special timed-release action . . . beneficial effect starts in minutes, lasts for hours.


first—the outer layer dissolves within minutes to produce 3 to 4 hours of relief
then—the inner core disintegrates to give 3 to 4 more hours of relief

Each* TRIAMINIC *Tablet provides:

Phenylpropanolamine HCl . . .	50 mg.
Pheniramine maleate	25 mg.
Pyrilamine maleate	25 mg.

One-half of this formula is in the outer layer, the other half is in the core.

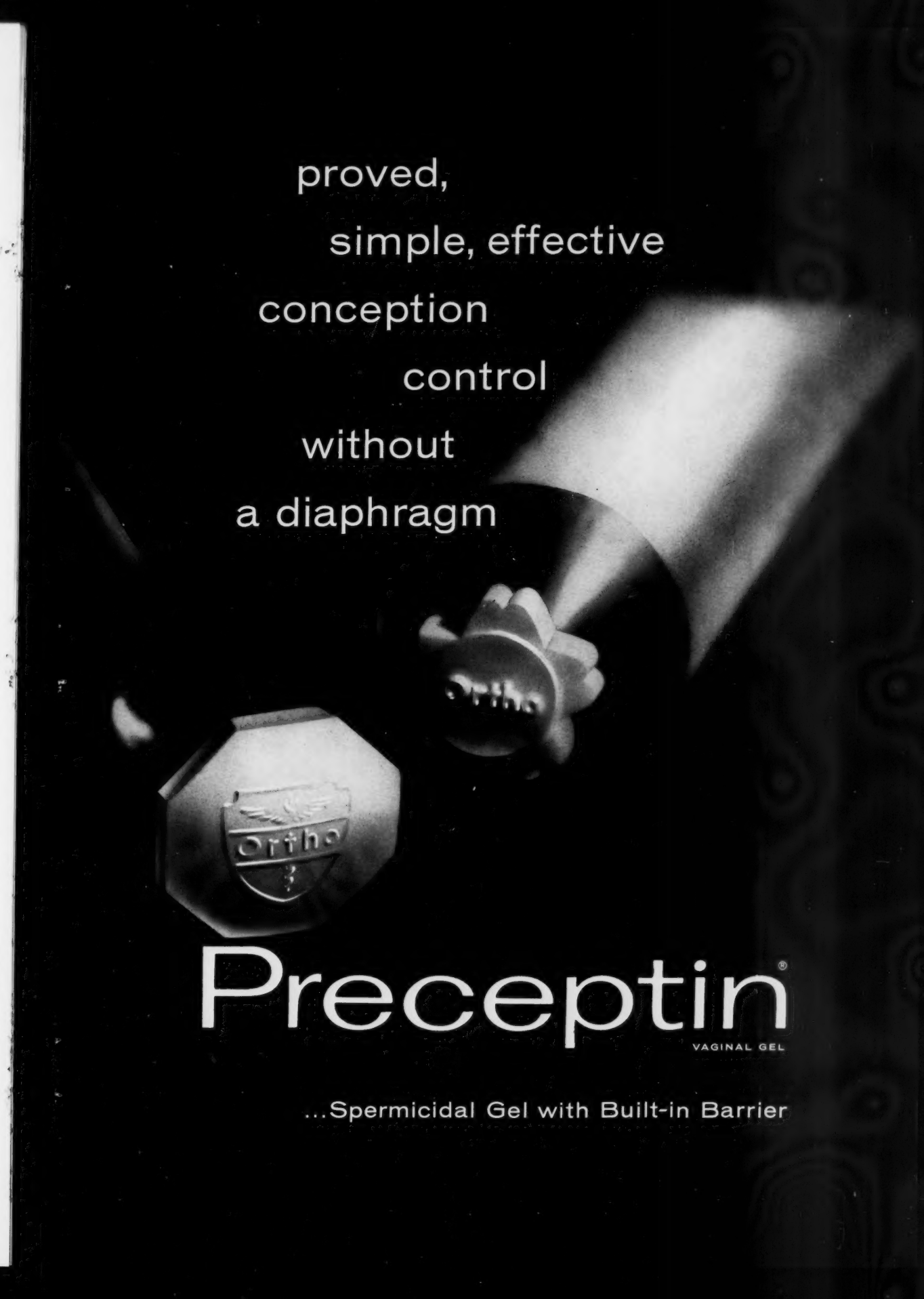
Dosage: One tablet in the morning, mid-afternoon and in the evening, if needed.

Triaminic®

Also available: For the occasional patient who requires only half dosage: timed-release TRIAMINIC JUVELETS. Each Juvelet is equivalent to ½ of a Triaminic Tablet.

For those patients who prefer liquid medication: TRIAMINIC SYRUP. Each 5 ml. tsp. of this palatable syrup is equivalent to ¼ of a Triaminic Tablet.

SMITH-DORSEY • a division of The Wander Company • Lincoln, Nebraska • Peterborough, Canada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Does not interfere with autonomic function
Does not impair mental efficiency,
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MEPROBAMATE (WALLACE)

Miltown®

Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets.

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